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THE CURABILITY OF CARCINOMA OF THE STOMACH

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THE surgical management of carcinoma of the stomach has improved greatly in recent years. The methods of diagnosis have been perfected. Cancer propaganda has been disseminated so that the public has become cancer conscious. Operative technique has improved and there have been marked advances in preoperative and postoperative care. Despite these encouraging signs which should indicate improved end results in the surgical treatment of cancer of the stomach, it is still true that gastric carcinoma presents the highest death rate and the lowest percentage of five-year cures of any type of malignant disease commonly treated by surgical means. However, surgery alone offers a hope of cure.

Implicated vitally in the mechanism of bodily nutrition, carcinoma involving the stomach tends to throw the patient into the group of poor surgical risks. This is reflected in the high operative mortality following palliative procedures or even simple explorations. Simple exploratory laparotomy for cancer of the stomach has a postoperative mortality of 15.5 per cent in this series of cases while gastroenterostomy, the most common palliative operation, has one of 25 per cent. As Ogilvie[1] suggests, when operating on patients for cancer of the stomach "we are working pretty near the limits of human endurance."

It has seemed important to us to consider these various factors together with their statistical effect on the treatment of carcinoma of the stomach as it has been observed in the Massachusetts General Hospital. This study is based upon the entire group of patients, 691 in all, who entered the Massachusetts General Hospital with this diagnosis in the ten-year period 1927-1936 inclusive. Five-year survival rates are calculated to and including the year 1933. This series will be compared

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with that previously reported by Parsons[2] from this hospital including the years 1922 to 1926.

In any consideration of a large series of cases of gastric neoplasm it is at once apparent that the opportunity given the surgeon for effecting any hope of cure is sharply limited by the natural course of the disease. Thus, as shown in Table I, of a total of 691 cases entering the hospital, 250, or 36 per cent, were either never offered surgery, refused it, or were too far advanced to warrant the risk involved in an exploratory laparotomy. Where operation was advised, about 35 per cent had resectable lesions and about 20 per cent of this group survived five years. To the problem of properly handling the cases once they are exposed to surgery is added the equally important factor of increasing the number of patients who have had an early diagnosis made and who are candidates for radical surgery.

TABLE I

	TOTAL CASES	NO OPERATION	EXPLORATORY LAPAROTOMY	PALLIATIVE OPERATION	SUBTOTAL RESECTION	TOTAL RESECTION
1927-31	296	115	55	58	68	0
1932-36	395	135	88	69	93	10
Total	691	250	143	127	161	10

Symptoms.—The problem of symptomatology involves the general practitioner and internist to a great, if not greater, extent than the surgeon. Now only 35 per cent of patients suffering from carcinoma of the stomach are able to have a resection performed or attempt at cure made; the progress in the control of cancer of the stomach in the future depends primarily upon increasing this percentage.

The material for study falls naturally into two groups according to the duration of symptoms. Unfortunately the larger group seems to have had symptoms for six months or less. Progressive weakness is the only prodromal sign. The onset of epigastric pain and vomiting indicates obstructive involvement of the pylorus and finally brings the patient to a physician. Until preventive medicine reaches a higher degree of efficiency whereby members of the general public after the age of 40 years receive a periodic x-ray examination of the stomach every six months, hope of progress in the future does not lie in this particular group.

It is true, however, that another large group of patients has digestive unrest for months or years before medical advice is sought. The advent of the radio in every home has placed at the disposal of every patient suffering from "upset stomach" a great variety of stomach sedatives. If the patient has not resorted to home treatment, he has, in most instances, been treated as a patient with probable gastric ulcer for varying periods of time. Obviously, not all gastric ulcers are malignant or

undergo malignant degeneration, but enough gastric carcinomas follow a history of preceding ulcer symptoms to regard all gastric ulcers as potentially malignant. Hampton and Holmes[3] have called attention to the frequent association of carcinoma with ulcer in the prepyloric area. Certainly in many cases a surgical operation has been performed for ulcer only to have the pathologist demonstrate malignant change in one area in the specimen. The pathologic department makes it a practice to take multiple sections through any gastric ulcer for this reason.

The observation that small gastric lesions often present distant metastases indicates a latent period in the development of the carcinoma. Epigastric symptoms suggestive of ulcer developing in a patient of middle age should be regarded as of neoplastic origin until the benign character is clearly established. With any change in the character of the symptoms or lack of improvement either clinically or by x-ray examination, carcinoma should be regarded as the probable diagnosis and surgery advised. Certainly the recognition of these early lesions will be necessary to increase the percentage of five-year cures, for it is in just this group that cure should be expected. Our experience is in accord with that of Balfour[4] who found that 35 per cent of patients who had had symptoms for over twelve months were living five years after resection, while only 25 per cent of those who had symptoms less than six months were living the same length of time.

Diagnosis.—The definitely increased percentage of operability in recent years indicates the fact that the diagnosis of cancer of the stomach is being made earlier. X-ray diagnosis, especially because of the employment of the spot film, has become more accurate in the differentiation of ulcer and cancer. The gastroscope has been of increasing value, especially for lesions in the fundus. With the advent of the peritoneoscope, another aid to diagnosis is presented. On the one hand, many patients with generalized carcinomatosis will be spared an exploratory laparotomy, while others may be made available for surgical treatment by excluding the possibility of numerous liver metastases. The discovery of ascites, extensive liver metastases, generalized carcinomatosis, or pelvic metastases with Krukenberg involvement of the ovaries, indicates that only a palliative operation can be performed. These factors may usually be determined by the peritoneoscope without the risk of an exploratory laparotomy. It is impossible to gain any indication of the possible fixation to the pancreas or liver by this means. The x-ray examination also is unreliable in the determination of fixation. With the practice of removing the entire omentum at the time of gastric resection, the presence of omental metastases visualized through the peritoneoscope cannot be regarded as a contraindication to surgery. On the other hand, metastases to the lung or supraclavicular area contraindicate any extensive procedure.

Preoperative Preparation.—Recent improvement in the preoperative preparation of patients for radical surgery has been definitely more marked than in the operative mortality of all types of operations for gastric cancer. Thus, the mortality for resection has diminished from 38 per cent to 25 per cent, for gastroenterostomy from 35 per cent to 25 per cent, and for exploratory laparotomy from 26 per cent to 15 per cent.

It is obvious that patients with gastric malignancy are cachectic beyond the point of observation. Vitamin deficiencies are frequently observed, and quantitive measure of cevitamic acid has shown the remarkably low vitamin C supply that is often present in these patients. Cevitamic acid can be brought back to normal within a few days by the proper administration of this vitamin. Wound healing may be influenced by the lowered cevitamic acid. Other vitamin deficiencies are in keeping with the ascorbic acid level.

A lowered serum protein is frequently observed and, if uncorrected, may contribute to edema of the stoma and a malfunctioning anastomosis. Transfusions are usually employed to correct this deficiency. A jejunostomy may be done for feeding purposes, but it may need to be maintained for a period of three weeks before complete relief can be expected. Secondary operations on the stoma or the jejunum near it are rarely, if ever, indicated.

Sepsis in the depleted patient increases in frequency as a lethal element as the scope for radical resection widens. Where culture of the gastric contents show beta-hemolytic streptococci, sulfanilamide may be tried. Frequent lavage with instillation of dilute hydrochloric acid has also been used. The value of these procedures is not definitely established, but repeated gastric lavages by means of the Levine tube are of great value in mechanical cleansing of the stomach.

Anesthesia.—Anesthesia is one of the chief factors in the mortality following gastric resection. Just as there are many surgical techniques employed by the various members of the staff of the hospital, so the choice of anesthetic has varied widely. Operations of gastrectomy, either total or subtotal, are followed by an unusually high incidence of pneumonia. The experience at the Massachusetts General Hospital has been chiefly with ether as an anesthetic. Avertin has been used as a basal anesthetic in many cases, but postoperative complications have been more frequent and relaxation has not been adequate. Using an intratracheal tube and ether administered through the closed circuit of the Gwathmey machine, adequate relaxation can be obtained with surprisingly little anesthetic. The average amount of ether used for a gastric resection varies between 1 and 2 ounces.

The routine use of local novocaine infiltration supplemented by the splanchnic block of Finsterer would undoubtedly reduce the postoperative incidence of pneumonia. Unfortunately, the temperament of most

of our patients is such that gas or ether must be used in addition. This combination we believe offers the most satisfactory method.

Spinal anesthesia has not been used to any extent in this hospital for gastric surgery. It is the opinion of our anesthesia department that the relatively high toxicity of nupercaine makes it an undesirable agent, while pontocaine cannot be relied upon to give an anesthesia of adequate duration.

Choice of Operation.—It was a point of interest in comparison between the group of cases reported in 1923 to 1926 and the present group to note the increase in the number of resections that have been done. It was possible to resect 16 per cent of all the cancers of the stomach entering the hospital from 1923 to 1926; this figure has increased to 25 per cent in the present series. However, it is of more practical importance to note the number of operated cases that can be resected. It may be seen from Table II that in the first series 27 per cent of all cases operated upon had a resection performed. This figure has increased to 37 per cent in the last ten years. Despite the increased number of resections, the operative mortality has been greatly lowered in the last five-year period so that in the last five years of this survey it was 25 per cent for all resections. That there is a definite mortality from cancer itself is shown by the fact that the operative mortality following exploratory laparotomy alone for cancer of the stomach has been 15.5 per cent in the last ten years; 20 per cent died of the disease while in the hospital for observation and medical care alone.

Certainly the so-called palliative operations of either anterior or posterior gastroenterostomy have little to recommend them, either from the point of view of longevity or comfort to the patient. The exclusion operation of von Eiselsberg involves a transection of the stomach above the growth, a turning in of the distal portion, and an anastomosis made with the uninvolved portion of the stomach. The advantage of this procedure lies in the fact that it permits a useful and satisfactory termination to a procedure begun with a high hope of cure which has become dissipated as complete fixation has been encountered. Certainly the patients have a greater degree of comfort after this operation than after a gastrojejunostomy. Palliative resections also frequently are done when it is impossible to remove metastatic disease. The removal of the local lesion in these patients provides greater comfort than could be obtained if the growth were left in place.

Resection alone offers hope of increased longevity or cure. Thus, the majority of cases should be considered as possible candidates for resection if the technical difficulties are not insurmountable. Radical surgery is contraindicated if massive metastases are present in the liver, but not if hepatic metastases are solitary or small. Resection is also inadvisable in the presence of ascites, metastatic disease in the supraclavicular area or the lung. Metastases in the pouch of Douglas or Krukenberg's tumors

of the ovary do not contraindicate a palliative resection. Involvement of the pancreas, duodenum, or transverse colon increases the technical difficulties and the question of resection is debatable, although a portion of these structures has frequently been purposely included in the resection when involved. The size of the growth gives no indication as to whether resection is advisable or not. Frequently the larger growths may remain confined to the stomach, while the smaller ones demonstrate distant metastases. The clinical evaluation of nodes about a gastric cancer is notoriously uncertain. Resection should never be abandoned because of the extent of supposed nodal metastases for the nodes may prove to be inflammatory. Likewise, the differentiation of cancer and ulcer at the time of operation may be impossible. It is our impression that resections should always be done in case of doubt. In the prepyloric area resection is always indicated. Gastric resection then should be done where technically possible except in the presence of extensive liver metastases, ascites, or massive involvement of vital structures where radical removal is not feasible.

Mortality.—The immediate operative mortality appears to vary in the five-year periods chosen for comparison as seen in Table II. The most encouraging sign is the improvement observed in the last five years where the mortality has dropped from a high of 43 per cent to the present level of 25 per cent. The reduction in this excessively high mortality rate is the essence of the problem of the surgical management of gastric cancer. Excluding operative mortality, one in three patients who have had a gastric resection for cancer survives five years.

TABLE II

	TOTAL CASES	TOTAL CASES OPERATED UPON	PERCENTAGE OF OPERATED CASES RESECTED	MORTALITY OF RESECTED (%)	FIVE-YEAR CURABILITY (%)*
1922-27	233	139	27	38	20
1927-31	296	181	37	43	21
1932-36	395	260	36	25	

*Includes operative deaths.

Pneumonia claims a third of the operative deaths. The anesthesia problem has been discussed and some degree of improvement may be expected with the wider use of local anesthesia. Special nursing with care directed toward the prevention of pulmonary collapse is of extreme importance. Bronchial aspirations either with a catheter or a bronchoscope may serve to remove mucous plugs before pneumonitis can develop behind them. If pneumonia develops, treatment with sulfapyridine or specific pneumococcus serum is indicated.

Peritonitis accounts for another third of the postoperative deaths. This looms high in palliative or extensive resections and will probably never be greatly lowered, due to the infection present in the growth.

The remaining deaths are due to miscellaneous complications. Operative shock, prominent as a cause of death in the early group, has been eliminated in late years by prophylactic transfusions. Pancreatitis occasionally causes death when it is necessary to remove a portion of that viscus. It is surprising that there were no fatal pulmonary emboli in this group.

Five-Year Survival.—The five-year survivals have been calculated through the year 1933. Twenty-one per cent of all patients who underwent resection from 1927 to 1933 survived the five-year period. This is essentially the same percentage that were cured by resection in the earlier study. It is to be noted, however, that, since resectability has increased from 27 per cent to 37 per cent, a much greater number of cures have been obtained. These cases represent 20 five-year survivals, or 4.6 per cent of all cases of carcinoma of the stomach that entered the hospital during that time. This is equivalent to 6 per cent of all cases operated upon. Of the cases that have been followed more than five years, 3 are known to have died of cancer, 1 six years, 1 seven years, and 1 nine years after operation. One patient is living ten years after operation, free of disease; 5, nine years, 2 eight years; and 1, seven years after operation. The others have survived from five to seven years. During this period there have been ten total gastrectomies performed for cancer. The longest period of survival was four years and eight months; death was due to recurrence. Since 1936, 20 additional total gastrectomies have been done in this clinic; these cases have been analyzed by Allen.

Certain interesting features appear in this group of cases. It is possible to divide them roughly into two groups: those who had symptoms longer than one year and those who had symptoms less than six months. Only 25 per cent of the survivors were found in the latter group. There is no significant difference in the ages of the two groups, nor were there any differential symptoms. In other words, rapidly growing cancers of the stomach are rarely cured, while cures are comparatively frequent in patients with long histories. Many of them may have originated from preceding ulcers. There is a definite ulcer story in 6 of the 20, while 4 of this group had prepyloric lesions. By x-ray examination the diagnosis of ulcer was made in 1 case, an equivocal diagnosis of ulcer or cancer in 4 cases, and a diagnosis of cancer in all the remainder.

At the time of operation only one of the involved stomachs had any fixation; this tumor was adherent to both gall bladder and pancreas and there were regional metastases. Of the 20 five-year survivals, 5 had metastatic nodes removed while 15 were free of metastases.

There is a marked difference in the curability of cancer of the stomach depending upon the extent of the disease. We have divided the cases of cancers observed from 1927 to 1933 that were resected into 3 groups. Group A includes those lesions that had no metastases, were

localized in the stomach, and were freely movable. In Group B the growth was still freely movable, but metastases were present in the regional nodes. In Group C the growth was fixed to a neighboring viscus,

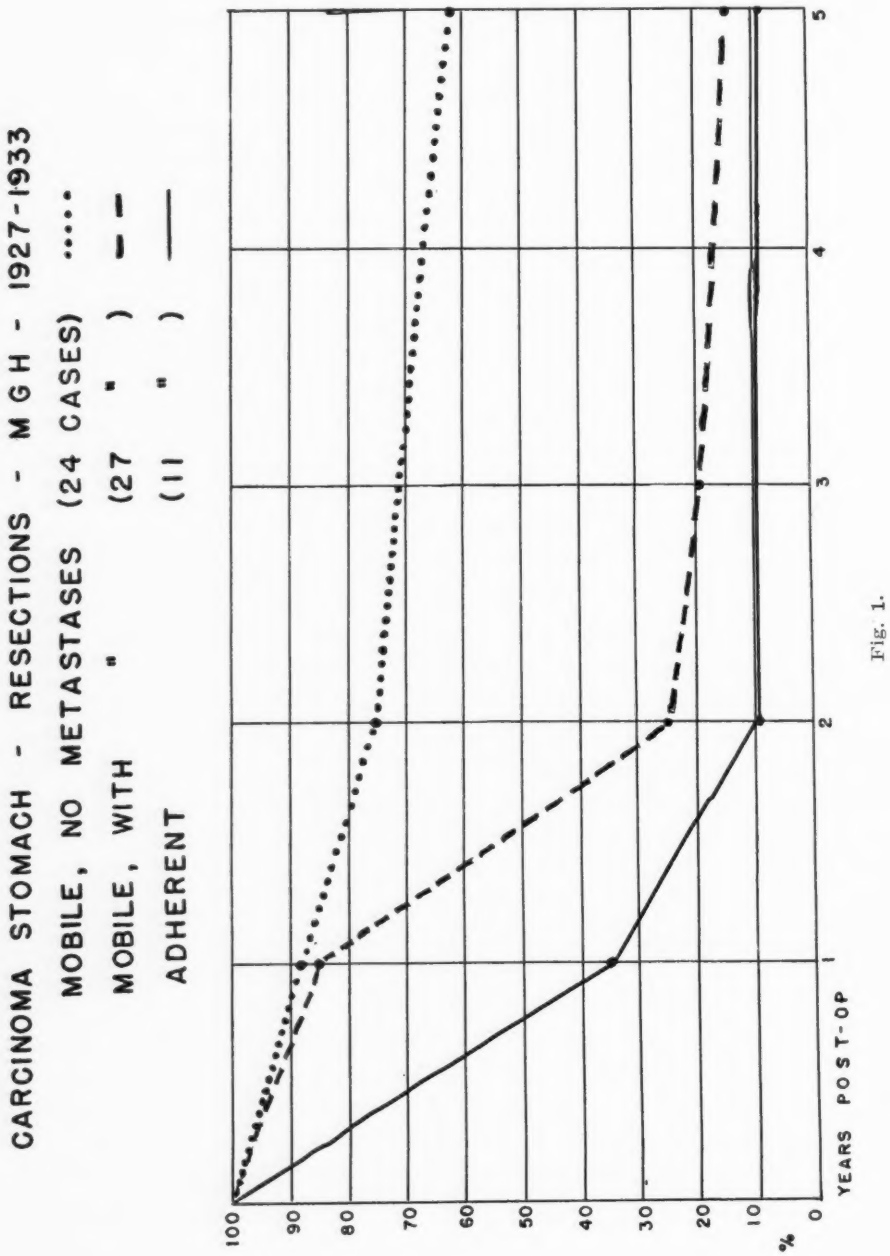

Fig. 1.

usually the pancreas. The survival rate is shown graphically in Fig. 1. Operative deaths are excluded in this graph. It indicates that a patient with a Type A cancer, if he survives the operation, has a 62 per cent

chance of living five years. If regional metastases are present, the chances drop to 18 per cent, while, if fixation is present, less than 10 per cent will survive this period. The importance of resection in early lesions of the stomach is strongly emphasized by these figures.

Ogilvie recently presented his experience with surgery for gastric malignancy as encountered in England in a most interesting diagrammatic form. Since the problem of surgical management of gastric carcinoma is a universal one, it would seem that a comparison of his experience with that of the Massachusetts General Hospital might be enlightening.

To compare our series with that of Ogilvie, Fig. 2 has been prepared. As a matter of convenience, 200 patients have been chosen as an arbitrary number. The ratio of the number of patients subjected to various operative procedures has been calculated in this way. Thus, 177 of our 691 patients, or approximately 50 of 200, had a resection done.

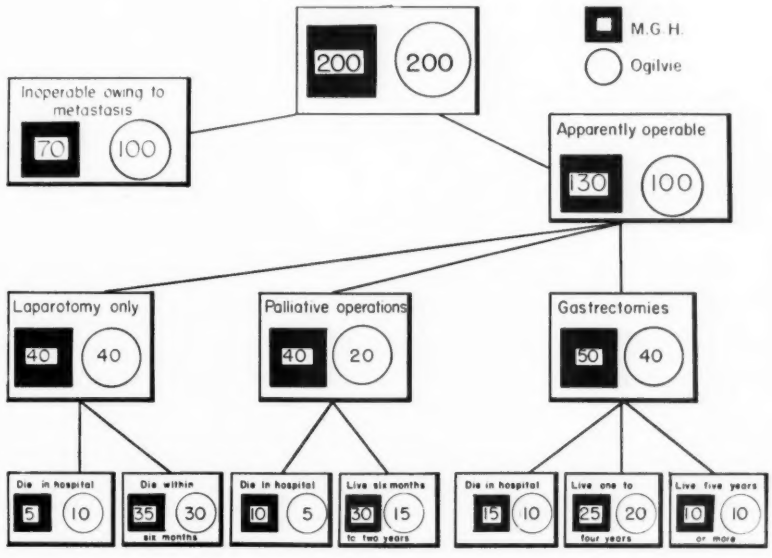

Fig. 2.

It is at once apparent that there is an immediate and appreciable difference in the cases selected as suitable for operation. That Ogilvie has selected well is readily appreciated when at the end of five years the total number of survivors is found to be the same in the two groups, although 30 per cent fewer cases were operated upon in his series.

The essential difference however would appear to be in the attitude taken toward the disease itself. If only those cases are to be chosen for operation with respect to five-year cure, it is reasonable that the indications for operation will be more restrictive. However, if some of the operative procedures, even to the extent of resection, are carried out with the idea of palliation, then of necessity more patients will be

offered operation. That this is aparently the case is made evident by observing twice as many palliative operations in the group from the Massachusetts General Hospital with twice as many survivors from six months

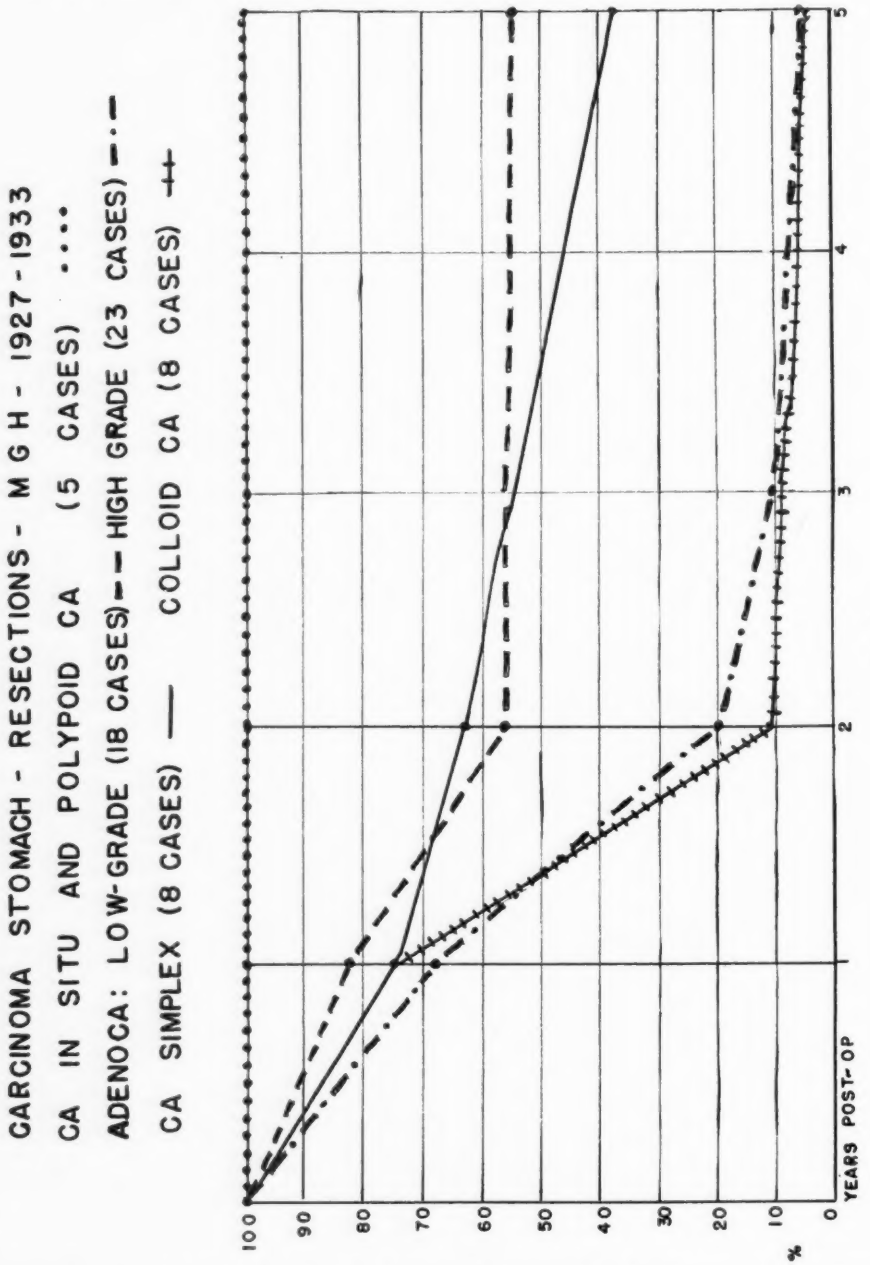

Fig. 3.

to two years following surgical interference. In the figure representing the number of resections, more resections are done in the Massachusetts General Hospital group with a larger immediate mortality but with

more patients alive one to four years after operation. In percentages the groups are exactly comparable except for a slightly higher immediate mortality in the series from the Massachusetts General Hospital, which possibly may be explained by the attempt to extend the indications for resection on the ground that enough patients are more comfortable after a resection or exclusion operation to justify the slight increase in the immediate operative mortality.

Except for the difference of opinion with respect to the value of palliation, the two sets of figures are astonishingly alike and may be regarded as representative of the problem of gastric carcinoma.

Pathology.—The pathologic sections of all the patients who survived operation, excluding a few slides that have been lost and in which the original report must be accepted, have been reviewed by Dr. Benjamin Castleman. The carcinomas have been divided into several different groups.

The least malignant is the carcinoma in situ. The cells of this tumor are definitely malignant, atypical in appearance, and with many mitoses. There is, however, no evidence of invasion below the basement membrane of the epithelium.

Adenocarcinomas are more malignant. Ranging from polypoid to highly invasive, all these cancers have more or less well differentiated acini. The Grade I adenocarcinoma is often polypoid and nearly as benign as the carcinoma in situ. Adenocarcinomas of Grades II, III, and IV are increasingly malignant.

The carcinoma simplex includes those cancers which are characterized by solid sheets of cells, without formation of acini. In the more malignant types, typical signet-ring cells are found. The colloid cancer is closely related to the signet-cell type; for practical purposes, these may be grouped together.

Review of these sections shows that all cases of carcinoma in situ who survived operation lived over five years. The only adenocarcinomas that lived five years after operation were either polypoid or of Grade I malignancy, with the exception of one Grade III adenocarcinoma. All but one of the cases of colloid cancer were dead before the end of the five-year period.

The 20 five-year cures included 3 carcinomas in situ, all prepyloric in location; 2 polypoid carcinomas; 11 adenocarcinomas, all but 1 of low-grade malignancy; and 4 cases of carcinoma simplex. Of the last group 2 are known to have died six and seven years after operation. One had a signet-ring type of carcinoma simplex and is still alive.

The prognosis according to the grade of cancer is graphically represented in Fig. 3.

SUMMARY

The total number of cases of cancer of the stomach that have been recognized has increased greatly in recent years. More patients have

been operated upon and the operability (i.e. resectability) has increased. Meanwhile, the operative mortality has been reduced. The percentage of five-year cures remains at approximately 20 per cent of all cases that have undergone resection, or approximately one-third of the patients who survive the operation. The prognosis is definitely influenced by the presence or absence of metastases and by the pathologic grading of the tumor.

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PULMONARY EMBOLISM

An Experimental and Clinical Study

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PULMONARY embolism is the cause of death in a small, but definite, group of cases. A number of large, collective series have been published; approximately 2 per cent of all deaths have been attributed to it and 6 per cent of postoperative deaths have been reported to be due to pulmonary embolism.[1] We are not concerned here with an analysis of these statistics nor with various efforts to prevent the formation of thromboses leading to a sudden obstruction of the pulmonary artery. An excellent review of the subject with a critical analysis of the clinical problems has been recently prepared by Barnes.[1] Rather, an experimental study has been undertaken here to analyze the mechanisms by which such emboli kill and to place the use of certain methods, which have been used clinically in the treatment of embolism, on a more rational basis.

EXPERIMENTAL STUDIES

The literature on experimental pulmonary embolism is vast and has been summarized in the monograph of Bardin.[2] Briefly, aqueous and oily suspensions of charcoal, lycopodium, solid masses consisting of fibrin, blood clots, cotton, paraffin, grains of rice, tapioca, starch, beads of enamel, mercury, and many other substances have been placed into a large vein of the animal. Such foreign bodies tend to plug the main artery, the larger branches or the peripheral arteriolar bed, and give rise to different trains of symptoms, depending on the size of the vascular bed which they occlude. Finally, ligatures and clamps producing partial or complete occlusion of the main artery have been applied. The study of Haggart and Walker,[3] undertaken in 1923, served as a model for later experiments and placed the amount of constriction necessary to produce death on a quantitative basis (an average of 64 per cent of the main artery). Gibbon and Churchill[4] pointed out that the experimental occlusion of the main artery corresponds to the syncopal type seen in man, which is characterized by pallor, low blood pressure, and normal oxygen saturation of the peripheral arterial blood; whereas, the

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asphyctic type, corresponding to the occlusion of the branches, is recognized by cyanosis, low oxygen saturation of the arterial blood, and a maintained or slightly lowered systemic blood pressure.

Churchill[5] discussed three possible mechanisms of death following pulmonary embolism; namely, (1) that of complete obstruction of the main artery with immediate death, (2) partial obstruction with delayed death due to reduced effective blood volume, and (3) partial obstruction with delayed death in which right heart failure is a component.

Most of these experiments, however, do not take into account: (1) the factor of anesthesia, which may modify important reflexes from the occluded segment; (2) that ligation of an artery is never comparable to an embolus at the same level; and (3) that the mechanism of death, which has been mostly regarded from a simple mechanical viewpoint, does not explain some of the fatalities in which only parts of the vascular tree are blocked.

In addition to the undoubtedly important mechanical considerations, one must consider certain reflex changes as contributory and occasionally deciding factors in the survival of the patient. In the last few years considerable experimental and clinical evidence has accumulated to show that the pulmonary vascular bed is richly supplied with sensory receptors[6] and that the pulmonary and bronchial vascular systems possess a strong vasoconstrictor mechanism which is under sympathetic control.[7] A group of investigators, stimulated by Sauerbruch's[8] paper before the German Surgical Congress in 1924, spoke of three mechanisms of death; namely, (1) acute asphyxia, (2) gradual right heart failure, and (3) immediate death in shock. This last they regarded as due to a sudden vagal stimulation producing cardiac standstill or coronary constriction. Mosler,[9] Scherf and Schönbrunner,[10] and Radnai and Mosonyi[11] presented electrocardiographic tracings following the production of pulmonary embolism and stated that surgical or pharmacologic block of the vagus improved the tracings and saved a number of animals. All of these authors believe that the pulmonary vagus produces a coronary constriction and thus brings on a syndrome hardly distinguishable from coronary occlusion.

A final group of investigators[12-14] concerned themselves with the depressor effects of the hypertonus occurring in the pulmonary artery, proximal to the obstruction. That hypertension of the pulmonary artery exists has been registered by Haggart and Walker[3] and emphasized by Churchill;[5] on the clinical side, White[15] has emphasized the acute cor pulmonale, but Schwiegk[12] supplied experimental data to prove that such a hypertonus is capable of initiating depressor reflexes mediated by a receptor mechanism similar to that of the carotid sinus.* His work was partly confirmed by Schweitzer.[13] This reflex would

*This structure sometimes is referred to as glomus pulmonum.[6]

bring about a fall in systemic blood pressure but also a decrease in coronary flow, which, according to Hochrein and Schneyer,[14] might vary in the two coronary arteries; measured with a Stromuhr, coronary constriction was seen more often in the right than the left coronary artery. The anatomic basis for the assumption of such sensory receptors was supplied by Takino and Watanabe.[16] With neurohistologic methods, they showed receptors in the wall of the artery, especially at the insertion of the obliterated ductus Botalli. Stimulation of this segment by the electric current or by distention resulted in a bradycardia and a fall in carotid pressure; when the left depressor or the left vagus nerve was cut, this effect disappeared. Depressor section produced degeneration of the receptors in the ductus Botalli; whereas, vagal section was followed by the degeneration of receptors in the left and right branches of the pulmonary artery.

Villaret, Justin-Besancon, and Bardin[17] are of the opinion that the reflex changes produced by emboli originate in the arteriolar tree and that small multiple emboli are much more dangerous in producing sudden syncope than a massive one. This does not agree with clinical observations.

This brief digest of more recent work on pulmonary embolism permits a well-grounded suspicion that not all patients die of the purely mechanical effects of a massive pulmonary block with a consequent right heart failure, diminution of cardiac output, and lack of circulating blood volume. It was our purpose in this study to (1) produce fatal pulmonary embolism of the massive and the multiple peripheral types in the experimental animal, (2) to find, if possible, certain measures which would protect the animals from death in at least a certain percentage of cases, and (3) to examine the possibility of clinical application. Studies of other angles of the problem are also in progress and will be reported later.

METHODS OF EXPERIMENTATION

After preliminary trials with pearl beads, B.B. shots, blood clots and wool threads, finally two methods were adopted, one to produce a multiple precapillary type and a second to produce a massive type of pulmonary embolism.

In the first group of thirty-five rabbits an emulsion of potato starch was injected into the central vein of the ear, using the method suggested by Dunn.[18] His solution was modified in that 8 gm. of starch shaken up with 17 c.c. of water seemed a suitable emulsion which could be readily injected and which produced death within five minutes in every case. The symptoms preceding death in order of their appearance were (1) dyspnea, (2) cyanosis, and (3) convulsions. The minimum

lethal dose was 2 c.c. Two cubic centimeters caused death in 100 per cent; 1.5 c.c. caused death in 30 per cent; and 1 c.c. caused no deaths. The sublethal dose produced dyspnea, cyanosis, restlessness, spontaneous micturition, and defecation. Within one-half hour, however, respiration, pulse, and color were normal, if the animal survived.

On autopsy, the main pulmonary vessels were always free. The starch granules were found impacted in the lobular arteries and some

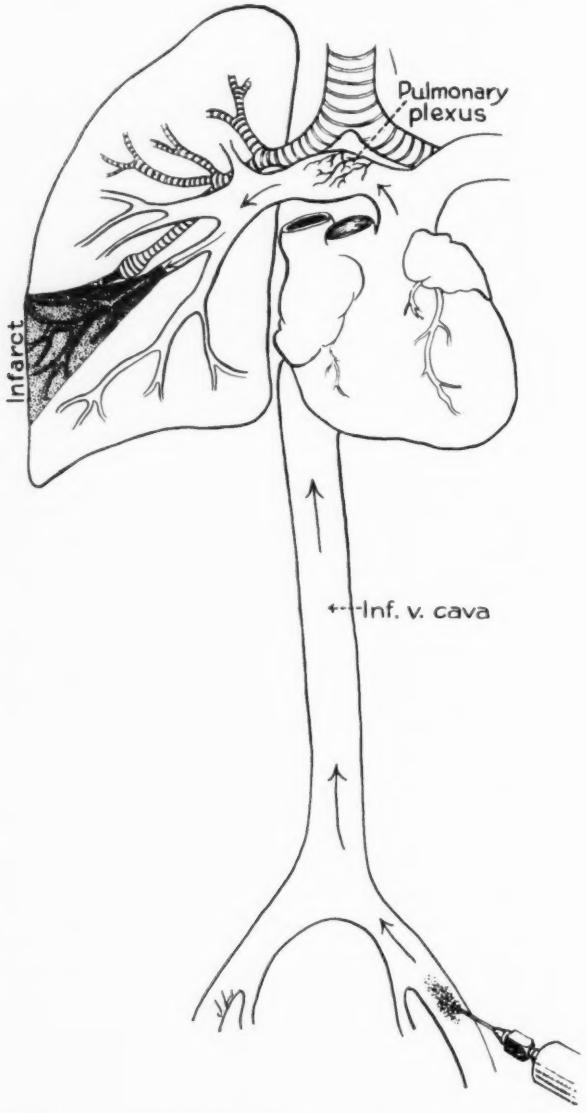

Fig. 1.—Diagram of experimental embolism produced with an emulsion of potato starch. Note the triangular infarct, which is well visible at immediate autopsy and which is almost invariably in the lower lobe. The right heart is not dilated, but there may be, dependent on the amount of peripheral vascular obstruction, a slight dilatation of the pulmonary artery. The bronchi are filled with blood and mucus in the infarcted area and are completely plugged, causing atelectasis. This type corresponds to a lung infarct in man, exhibiting cyanosis and dyspnea but no fall in blood pressure.

of them in the wall of the alveoli. They were readily identified by the starch-iodine reaction. The size of the granules varied from 50 to 150 microns, thus corresponding to the size of the arterioles. Distal to the multiple plugs, the capillaries were filled with blood, and free blood was seen in the alveoli and the smaller bronchi. The trachea and larger bronchi were filled with bloody mucus. There was evidence of interstitial edema and hemorrhage. (Fig. 1.)

As it was felt that the size of the starch granules was variable and might not always give the identical amount of arteriolar obstruction, a 1 per cent aqueous emulsion of lycopodium spores was injected in another series of rabbits. The size of the spore was quite constant, between 40 and 60 microns, thus producing a precapillary plug. It took from 10 to 15 c.c. of this solution to produce death within a short time and the solution was difficult to inject.

The embolism produced with potato starch simulated the peripheral, precapillary type of embolism. Its main symptoms were cyanosis and dyspnea. As shown previously by Dunn[18] and Singh,[19] the dyspnea is not due to oxygen want or to the irritating action of the embolic material; or, as Binger, Boyd, and Moore[20] believe, to the chemical changes in the blood or to the rise in pulmonary pressure. Harrison and his co-workers have pointed out, however, that the pulmonary afferent fibers of the vagus nerve are extremely sensitive to pulmonary congestion.[21, 22] In a second series of ten rabbits, gr. $\frac{1}{6}$ of atropine was given intravenously just before the injection of starch. The atropine did not protect these animals from death, but the dyspnea was absent and the bronchial tree was remarkably free from mucus.

In a third series of ten rabbits, oxygen was administered by tracheal intubation. This procedure also reduced the dyspnea and protected the whole series from death when the 2 c.c. dose was given. It was necessary to give a 4 c.c. dose to produce fatality in every instance.

While systemic venous and arterial pressures were not measured in every experiment, the few measurements obtained showed that they were essentially unchanged.

In a final series of ten rabbits, drugs were used which are known to be bronchial dilators, as a bronchial spasm was shown to be present

TABLE I

RESULTS OBTAINED FOLLOWING PRODUCTION OF PERIPHERAL TYPE OF PULMONARY EMBOLISM

SERIES	NUMBER OF ANIMALS	LETHAL DOSE	MEDICATION	REMARKS
1	35	2 c.c.	None	Dyspnea, cyanosis
2	10	2 c.c.	Atropine	Dyspnea relieved but all died
3	10	4 c.c.	Oxygen	Dyspnea and cyanosis reduced
4	10	2 c.c.	Epinephrine	Pulmonary edema
5	10	2 c.c.	Papaverine	Bronchi free; sedation marked

in Singh's experiments.[19] Adrenaline, amylnitrite, sodium nitrite, and papaverine were used. They were unable to protect the animal from death in the dosage employed; the bronchi were free, but pulmonary edema was especially marked after the use of epinephrine. This has been previously noted by a number of observers[23] (Table I).

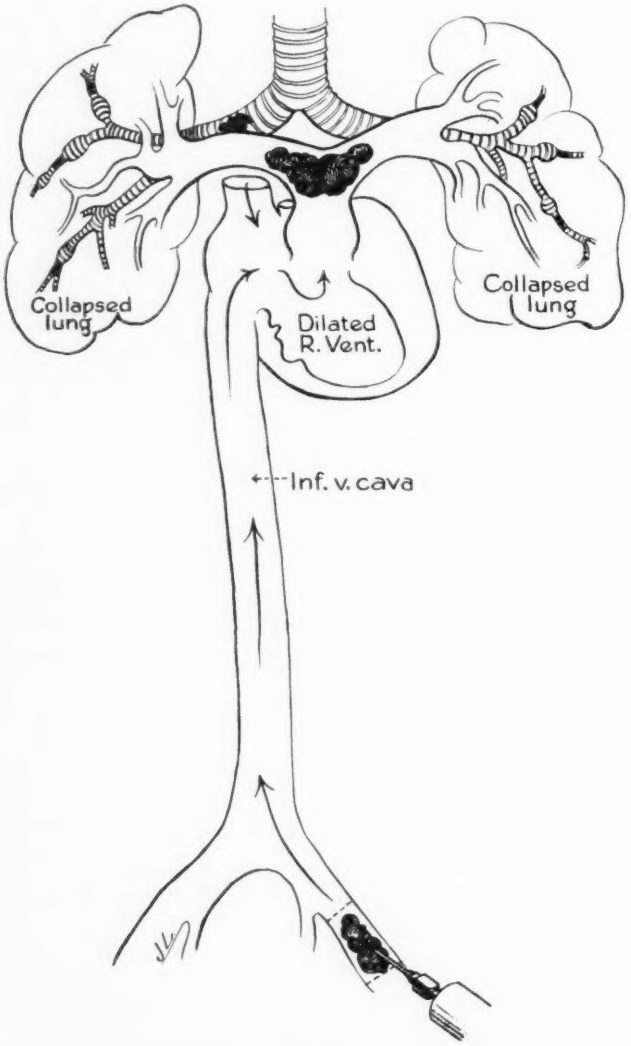

Fig. 2.—Diagram of experimental pulmonary embolism produced with Martin's solution and causing a massive plug in the main pulmonary artery. Note the "cor pulmonale," the dilatation of the right breast, and the multiple plugs in the bronchial tree. The lungs are more often collapsed and atelectatic, but may be edematous. Death occurs suddenly with a marked fall in blood pressure, pallor, and hardly any cyanosis. This corresponds to the syncopal type of embolism.

In the second group, dogs were employed and to simulate massive pulmonary embolism the solution of Martin was used.[24] An emulsion of iron perchloride, 1 part; normal salt solution, 1 part; and barium sulfate, 15 parts, was the original formula. This we have gradually

changed to 3 equal parts of the ingredients, as the emulsion was easier to inject and we were not interested in visualizing the clots by x-ray, except in a few instances. The femoral vein was exposed at Poupart's ligament for a length of about 1 cm.; it was compressed proximally while the emulsion was injected and the compression was maintained for fifteen seconds, after which it was suddenly released. The embolus was then exactly the length and width of the exposed venous segment and only seldom grew by apposition. In the small dog it corresponded to the size of the pulmonary artery. It could be readily distinguished from post-mortem clots by its gritty, granular appearance due to the barium (Fig. 2). If it was kept in contact with the femoral vein for longer than twenty seconds, parts of it might firmly adhere to the wall of the vein and the emboli were not of uniform size.

A series of twenty-five dogs, weighing less than 12 kg., all died within a few seconds to less than five minutes, when 2 c.c. of the emulsion were injected. Death occurred with extreme pallor, hardly any cyanosis, but again marked dyspnea. In the few instances in which blood pressures were taken from the carotid artery, the pressures fell very rapidly; whereas, venous pressure rose. This obviously was the type described by Sauerbruch, Rochet, Gibbon, and Churchill as the syncopal type of embolism. On autopsy the plug was in the main pulmonary artery or its major branches. The right heart was markedly distended and pulmonary hypertension was obvious. X-rays of the heart obtained before and after embolism illustrated the sudden dilatation of the right heart.

In a second series of twenty-five dogs, gr. $\frac{1}{5}$ of atropine was injected intravenously a few minutes prior to the production of the embolus. Seventeen out of the twenty-five dogs survived more than ten minutes, some of them living from two to twenty-four hours.

Ten dogs were prepared by bilateral vagal section prior to the injection of the femoral vein, and four out of the ten survived for several hours. This series, however, is too small to permit any conclusions.

Dogs treated with sodium nitrite or with adrenaline all died. The dogs receiving 1 c.c. of adrenaline intravenously showed a marked pulmonary edema with a frothy mucus pouring out of their mouths and nostrils. Papaverine saved over one-half of the animals; its sedative action was marked (Table II).

TABLE II

RESULTS OBTAINED FOLLOWING MASSIVE TYPE OF PULMONARY EMBOLISM

SERIES	NUMBER OF ANIMALS	PREVENTION	FATALITY	REMARKS
1	25	None	100%	Pallor, syncope, dyspnea
2	25	Atropine	32%	
3	10	Vagotomy	60%	
4	10	Epinephrine	100%	Marked pulmonary edema
5	10	Papaverine	40%	Sedation marked

ELECTROCARDIOGRAPHIC FINDINGS

Continuous electrocardiograms are available in fifteen of the experiments. In all cases the tracings were made with the dogs lying in the same position and no alteration was made in the electrodes. The tracings arranged themselves generally into four groups, as follows: (1)

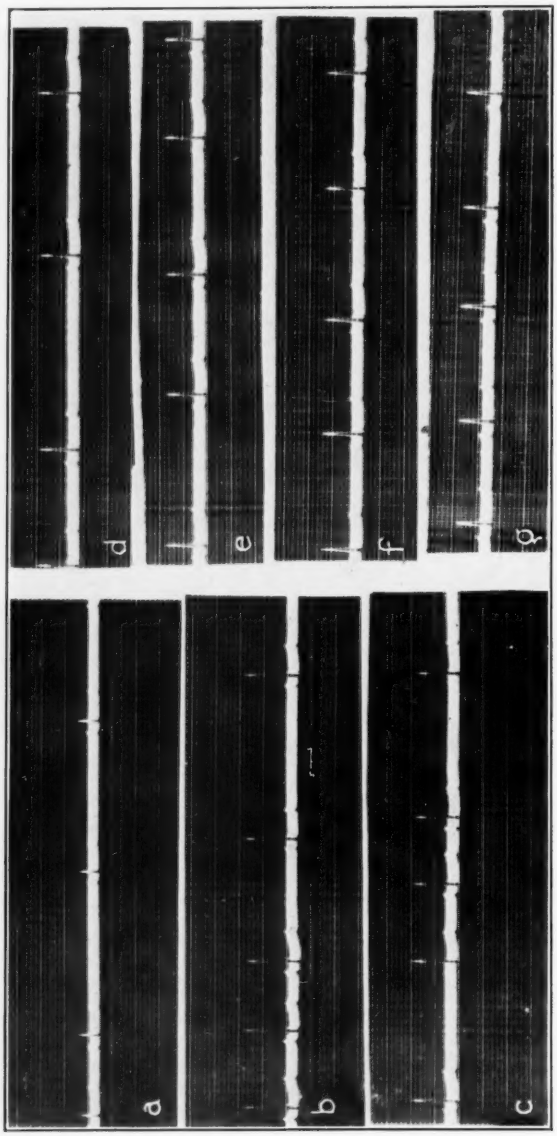

Fig. 3.—Electrocardiogram of Dog 70 weighing twenty pounds. Two and one-half cubic centimeters of Martin's solution were given. There were no clinical or electrocardiographic changes during the following twenty minutes. *a*, Control Lead I; *b*, control Lead II; *c*, control Lead III; *d*, Lead II immediately following 2.5 c.c. of Martin's solution; *e*, Lead II five minutes later; *f*, Lead II ten minutes later; and *g*, Lead II twenty minutes later.

no clinical symptoms and no electrocardiographic changes; (2) no clinical symptoms but slight electrocardiographic changes; (3) marked electrocardiographic changes followed by death; (4) marked electrocardiographic changes followed by recovery.

Fig. 3 represents an example of the first group. Dog 70 received 2.5 c.c. of Martin's solution and there were no clinical or electrocardiographic changes during the following twenty minutes.

Fig. 4 represents an example of the second group. Dog 35 received 1 c.c. of Martin's solution without clinical or electrocardiographic symptoms, but following the injection of a second c.c. of the solution there was a definite inversion of the T-wave, although clinical signs were still absent.

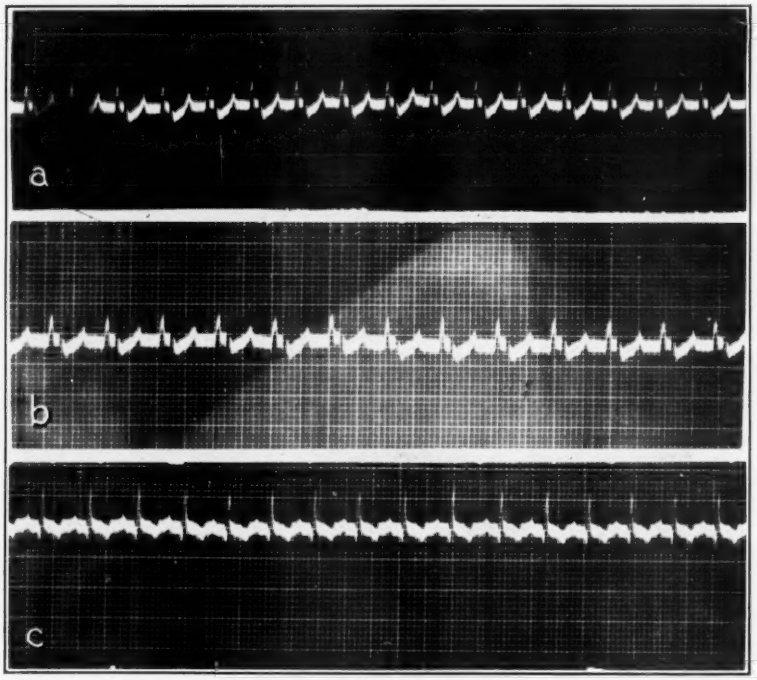

Fig. 4.—Dog 35 received 1 c.c. of Martin's solution into the femoral vein without any clinical symptoms or changes in the electrocardiogram; following the injection of the second c.c., there was a definite inversion of the T-wave, although clinical signs were absent. *a*, Lead II, control; *b*, Lead II after 1 c.c. of Martin's solution; and *c*, Lead II after 2 c.c. of Martin's solution.

In Groups 3 and 4 marked electrocardiographic changes occurred and these changes arranged themselves in the same general pattern. First, there was aberration of the S-T segment, either elevation or depression. This was followed by a slowing of the heart rate with a change in rhythm. These rhythm changes included nodal rhythm, partial A-V dissociation, complete dissociation, and idioventricular rhythm.

Dog 27 represents an example of the third group (Fig. 5). Within a few seconds following the injection of 2 c.c. of the iron chloride, the pacemaker appeared to be dislocated into the A-V node and there was marked depression of the S-T segment. Twenty seconds later an abrupt cardiac standstill appeared which persisted for about thirty seconds. Cardiac action reappeared with the pacemaker still in the A-V node and the S-T segment still markedly depressed. From this

point on, it seems impossible to interpret accurately the mechanism through its rapid changes. It seems most likely that the pacemaker remained at or near the A-V node and continued thus until the dog died a few seconds later. It is possible that there was a short period of idioventricular rhythm with retrograde conduction for a period of about 20 seconds.

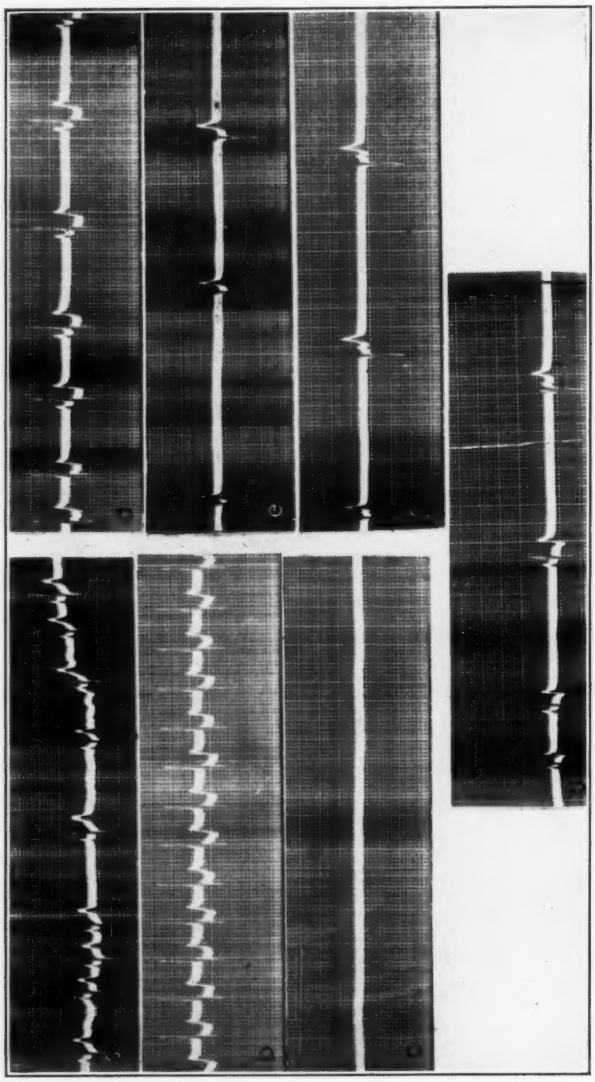

Fig. 5.—In Dog 27, within a few seconds following the injection of 2 c.c. of the iron-barium solution, the pacemaker appears to be dislocated into the A-V node and there is marked depression of the S-T segment. Twenty seconds later an abrupt cardiac standstill appeared and persisted for about thirty seconds. Cardiac action reappeared with the pacemaker still in the A-V node and the S-T segment still markedly depressed. From this point on, it seems impossible to accurately interpret the mechanism through its rapid changes. *a*, Lead II, control; *b*, Lead II immediately after 2 c.c. of Martin's solution; nodal rhythm with marked depression of S-T segment; *c*, Lead II twenty seconds later; complete cardiac standstill; *d*, Lead II ten seconds later; recovery, first in A-V node and later in S-A node; *e*, Lead II twenty seconds later; idioventricular rhythm; *f*, Lead II ten seconds later; idioventricular rhythm with auricular responses; *g*, Lead II ten seconds later; return to S-A rhythm and then back to idioventricular rhythm; later cardiac standstill and death.

Fig. 6, Dog 28, represents a similar series of events, but with recovery. Immediately following the injection of the solution, a marked nodal tachycardia appeared, accompanied by retrograde conduction and elevation of the S-T segment. Atropine, gr. $\frac{1}{6}$, was given; idioventricular rhythm and five seconds later a cardiac standstill occurred. This persisted for about eighteen seconds and cardiac activity began once more

with idioventricular rhythm. Thirty-three seconds later the auricular complexes reappeared but complete dissociation persisted. After a second injection of atropine, the rhythm changed to a high degree of partial block. With succeeding tracings, sinus rhythm was established with all beats conducted and the dog recovered.

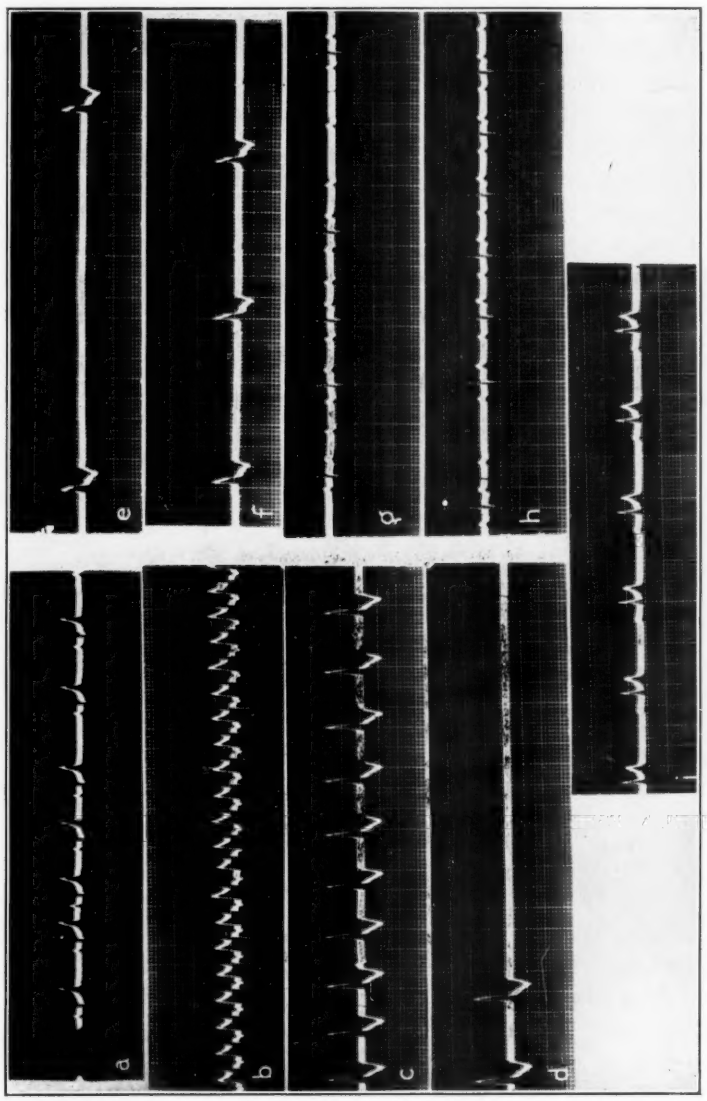

Fig. 6.—Dog 28 represents a similar series of events as those shown in Fig. 5, but with recovery. Immediately following the injection, a marked nodal tachycardia, retrograde conduction, and elevation of the S-T segment appeared. Atropine, gr. 1/6, was given intravenously. Idioventricular rhythm and, five seconds later, a cardiac standstill occurred. This persisted for about eighteen seconds and cardiac activity began once more with idioventricular rhythm. Thirty seconds later the auricular complexes reappeared, but complete dissociation persisted. After a second injection of atropine the rhythm changed to a high degree of partial block. With succeeding tracings, sinus rhythm was established with all beats conducted. The dog recovered. *a*, Control; *b*, immediately after 1.5 c.c. of Martin's solution; nodal rhythm with marked elevation of the S-T segment; *c*, 10 seconds later; idioventricular rhythm; atropine, gr. 1/6, given; *d*, 5 seconds later; cardiac standstill; *e*, 18 seconds later; recovery; idioventricular rhythm; *f*, 33 seconds later; idioventricular rhythm; auricular complexes reappear; *g*, 20 seconds later; S-A rhythm with high degree of A-V block; *h*, 20 seconds later; S-A rhythm with lesser degree of A-V block; second dose of atropine, gr. 1/6, given; *i*, 2 minutes later; S-A rhythm with elevation of the S-T segment; third dose of atropine, gr. 1/6, given, ½ minute preceding this tracing; dog recovered.

COMMENT

In this group of experiments no attempt was made to study systemic and pulmonary blood pressures, blood gases, or to determine coronary blood flow, although occasionally we have made such determinations. These determinations would not be available in clinical cases. Rather we wished to test some simple clinical methods as to their efficacy in

preventing death. In the asphyctic type of embolism, brought about by multiple miliary emboli, oxygen inhalations were definitely protective. Contrary to the statement of Villaret, Justin-Besancon, and Bardin,[17] these peripheral emboli were not initiating any important depressor reflexes which might be suppressed by atropine, as atropine is not protective in this series, except that it inhibits dyspnea. Whether dyspnea is a useful or useless mechanism here cannot be stated with certainty, but its suppression by atropine is definite.[21, 22] To relieve the bronchial spasm, which no doubt adds to the difficulty of free respiration, epinephrine or ephedrine seems logical. Papaverine acts directly on smooth muscle; its action on bronchial musculature has been shown by Macht[25] and on the coronary circulation by Rössler.[25] Papaverine seemed to be superior to epinephrine or ephedrine, as it does not raise the pressure in the pulmonary artery and is known to relax smooth muscle of the vessels and bronchi; nor does it produce an undesirable fall in systemic blood pressure as the nitrites do.

Atropine, on the other hand, is our most effective inhibitor of vagal and depressor reflexes; it furthermore stimulates the respiratory center, which may be insufficiently oxygenated during the syncopal attack of pulmonary embolism. Its action on smooth muscle must be slight. Oxygen inhalations naturally combat cyanosis and raise the low oxygen saturation of the arterial blood. Adrenaline and neosynephrine, while they may suddenly raise the low systemic blood pressure, do more harm than good in our opinion. Epinephrine caused marked pulmonary edema by increasing pressure in the pulmonary artery[26] and by increasing sympathetic vasoconstriction of the pulmonary vascular bed;[7] neosynephrine has a strong vagal action and is capable of producing a partial heart block in individuals whose vagal endings are sensitized;[27] this drug, together with digitalis and strophanthin, may well increase the vagal tone, which we are trying to suppress with atropine.

Venesection, in the absence of shock, has been suggested by White[15, 28] and practiced by some French authors to relieve the acute cor pulmonale; it is true that it might relieve the distention of the right heart temporarily, but it might precipitate the impending shock; it would not relieve the obstruction and the same pressure would be built up again as long as the right heart is capable of contracting.[29] The fall in systemic blood pressure is one of the mechanisms which spares the right heart from overdistention[12] and within certain limits (perhaps to 70 or 80 mm. of mercury) need not be treated.

It seems to us that any procedure which would diminish the increased blood pressure in the pulmonary artery should be helpful in combating death from pulmonary embolism. Of papaverine, we know it relaxes smooth muscle and it has been found to release vascular spasm in peripheral arteries; it has been found helpful in the bronchial spasm of asthmatics and there is some evidence of bronchial spasm in pul-

monary embolism.[19] Atropine decreases the depressor reflexes originating from the pulmonary hypertonus and also decreases dyspnea. The combination of these drugs should be helpful in certain cases of pulmonary embolism.

The interpretation of the electrocardiographic findings is difficult. It will be noted that Lead II of the electrocardiogram was used to follow the changes. All of the small dogs receiving adequate doses of Martin's solution died within a few seconds to five minutes unless they were protected with atropine. In an effort to obtain an almost continuous tracing from the time of injection until death or obvious survival, the single lead was used. It is possible that more accurate information might be gained by including additional leads, and such observations are being carried on in an additional series of experiments.

From the present series of experiments it is impossible to say without argument just what produced the electrocardiographic changes. The type of curve produced is that which is consistent with interference with the coronary circulation. If we assume this hypothesis to be true, we are still unable to say just what produced such interference. Three possibilities immediately suggest themselves. First, a reflex vagal inhibition of the heart; and second, peripheral vascular collapse arising from the pulmonary hypertension through the depressor nerve. There can be no doubt that peripheral vascular collapse occurred in many of the animals, as is shown by the rapidly falling systolic blood pressure. This depressor effect from the pulmonary artery must predominate over the reflexes from the right auricle, carotid sinus, and aorta, all of which would tend to oppose the fall in blood pressure. Whether this collapse was a primary affair or whether it was consequent upon decreased coronary flow cannot be determined from these experiments. The third possibility is acute right ventricular failure due to mechanical interference with the pulmonary circulation which again obviously interferes with coronary flow.

In considering all of these possibilities, the first holds out the most attractive features. Electrocardiographic changes occurred in some animals that showed no sign of shock or of right ventricular failure (Fig. 4). That changes in intrapleural pressure,[21] in intrapulmonic pressure,[30, 31] and in pressure of the pulmonary artery[12, 13] elicit depressor reflexes is well established. A combination of the first two mechanisms must be seriously considered. The purely mechanical effect of the dilatation of the right heart as the cause of the electrocardiographic changes has been brought forward by White[15] and Love, Brugher, and Winslow.[32] Measurement of the coronary flow is now being carried out and may throw some light upon this question.

That profound vagal stimulation took place seems clearly indicated by the rhythm changes. Dislocation of the pacemaker from the sinus node, A-V rhythm, partial block, complete dissociation, and complete

suppression of the auricle with idioventricular rhythm are all indicative of strong vagal effects.

In addition, it will be noted that all of the untreated dogs that received effective doses of Martin's solution alone died rather promptly. Many of those receiving effective doses of this solution plus atropine survived. The electrocardiographic changes shown in Fig. 6 immediately following the production of the embolus were quite comparable to those in Fig. 5. After the administration of a considerable dose of atropine, these changes were reversed and passed by steps back to a normal sinus rhythm, although the coronary type of curve still persisted.

This work was completed when the interesting study of Love, Brugher, and Winslow appeared.[32] They used clotted blood, colored with India ink, to produce pulmonary embolism in the animal and came to the conclusion that the changes in the electrocardiogram observed after pulmonary embolism are due to dilatation of the right ventricle and that the changes are essentially the depression of the S-T segments in one or more leads. This was found to be true most often in Lead II and often the reversal of the direction of the T-waves in Lead III and the precordial lead were observed. They felt that myocardial anoxemia or reflexes mediated through the autonomic nervous system play no role in the production of the electrocardiographic changes. The depression of the S-T segment was also produced on ligating the pulmonary artery, but not following hemorrhage, shock, or coronary injury. Love, Brugher, and Winslow quote one vagal section experiment in confirmation of their belief, which does not inhibit widespread axon reflexes within the vagal distribution. The existence of these has been suggested by O'Shaughnessy[46] and Hochrein and Schneyer.[14]

CLINICAL APPLICATION OF RESULTS

In trying to apply the experimental observations in the treatment of pulmonary embolism, two questions immediately present themselves: (1) how accurate is the diagnosis of pulmonary embolism and (2) is there time enough between the onset of clinical symptoms and death to utilize some of the procedures tested in the animal?

Nygaard[33] has made a searching inquiry of the material which came to autopsy at the Mayo Clinic from 1921 to 1933. Of 289 cases of death due to postoperative pulmonary embolism, a correct diagnosis has been made in 82.35 per cent, while the diagnosis was missed in 17.65 per cent. In these 51 cases the causes of death in order of frequency were (1) cardiac failure and coronary occlusion, (2) indeterminate diagnosis, (3) shock and hemorrhage, (4) peritonitis, (5) pulmonary edema, (6) coma, (7) cerebrovascular accidents, and (8) other conditions. It is obvious that the smaller emboli will give a more confusing picture than the massive embolus obstructing both pulmonary arteries.

Statistics giving the reverse side of the picture, namely, the percentage of pulmonary emboli causing death but erroneously diagnosed, are more difficult to obtain. But it is well known that the cause of death from pulmonary embolism, as determined at post mortem, is from 2 to 6 per cent; whereas, the clinical diagnosis of pulmonary embolism, especially in the nonsurgical cases, is much lower. One then has to study the hospital records for early signs and symptoms of proved cases of pulmonary embolism. This we have done in taking 100 cases of pulmonary embolism from the records of St. Luke's and Research and Educational Hospitals. As Barnes pointed out, it is necessary to avoid the obsession that cyanosis and dyspnea are the cardinal signs of pulmonary embolism.

The variation in the time interval between the first symptoms and death has been discussed repeatedly. We only quote some of the recent statistics. Shambaugh[34] reviewed 92 cases of fatal pulmonary embolism which occurred at the Peter Bent Brigham Hospital. Of the 92 patients, 33 were found dead or died shortly after the initial symptoms; 36 survived from ten minutes to one hour; and 15 survived from one to twelve hours. Robertson[35] tabulated the clinical signs and symptoms of 146 cases dying of pulmonary embolism and found that 39 per cent gasped, fainted, became pallid, and died within one hour; whereas, 61 per cent had chest pain, cyanosis, and hemoptysis and lived several hours or days. Obviously the latter is the asphyctic, the former the syncopal type of embolism and the symptoms vary according to the site of the arterial obstruction. Our own figures, to be published elsewhere in detail by Jesser and one of us (de Takats), indicate that if one utilizes the nurses' records for the detection of prodromal signs and symptoms, the interval between the initial symptoms and death is longer than has been reported in other series. Table III summarizes the time

TABLE III

INTERVAL BETWEEN FIRST CLINICAL SYMPTOMS AND DEATH FROM FATAL PULMONARY EMBOLISM (70 CASES)

TIME ELAPSED BETWEEN FIRST SYMPTOMS AND DEATH	
Found dead or died immediately	3
Ten min. or less	3
From 10 min. to 1 hr.	16
From 1 to 12 hr.	20
From 12 to 24 hr.	4
From 1 to several days	24
Total	70
Died in less than 10 min.	8.5%
Died in less than 1 hr.	31.0%
Died in more than 1 hr.	60.5%

interval which elapsed between the first symptoms and death following pulmonary embolism. It will be remembered that when Trendelenburg first described embolectomy from the pulmonary artery, he stated that approximately 50 per cent died before any kind of help could be administered; in Shambaugh's series about one-third of the patients died sud-

denly or within ten minutes to a day; whereas twenty-four patients, approximately one-third of all cases, lived from one to several days. This latter group, the slowly fatal pulmonary embolus, had either repeated infarcts or showed evidence at post mortem of a progressive thrombosis in the pulmonary artery, not unlike the descending thrombosis one sees following peripheral arterial embolism. Belt[36] has especially emphasized that pulmonary embolism is a recurrent event with repeated migration of a blood clot over a period of hours or days.

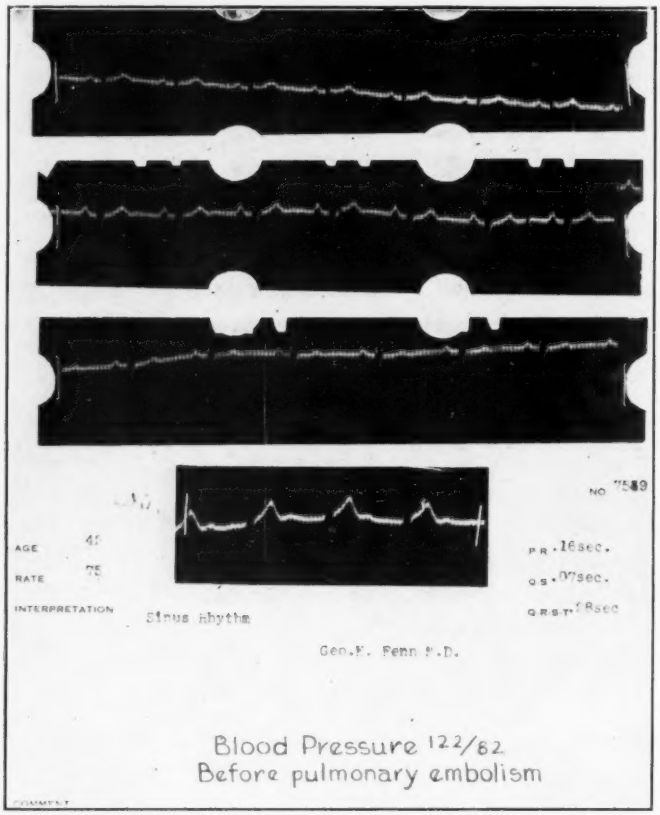

Fig. 7.—Electrocardiogram of G. P., 35-year-old male, previous to a lumbar sympathectomy undertaken for Buerger's disease. It shows a normal tracing.

One can emphatically state then that, provided the nursing and intern staff are made embolism conscious, a large majority of patients, sixty-four out of seventy proved cases in our series, live longer than ten minutes, so there is an opportunity to adopt some therapeutic measures. As Nygaard[33] has pointed out, the possibilities of a successful embolectomy are very slight. The Trendelenburg operation has been carried out up-to-date 132 times with a mortality of 93.2 per cent. It must be pointed out, however, that these embolectomies were all performed on the rapidly fatal cases; the slowly fatal cases, as recently suggested by Pilcher,[37] might be operated on two to three hours after the onset of symptoms while not in a moribund state.

The use of drugs to combat pulmonary embolism started with papaverine. Burk,[38] Denk,[39] de Takats,[40] and Collins[41] have published reports on patients who were seemingly saved by the intravenous administration of papaverine or "eupaverine," a close derivative of it. These recoveries promptly bring up the question of the percentage of spontaneous recoveries from massive pulmonary infarcts. We have studied the histories of thirteen patients in whom the clinical symptoms, rusty sputum or pure hemoptysis, pleural friction rub, signs of pulmonary consolidation, and x-ray evidence of an infarct made the diagnosis of a

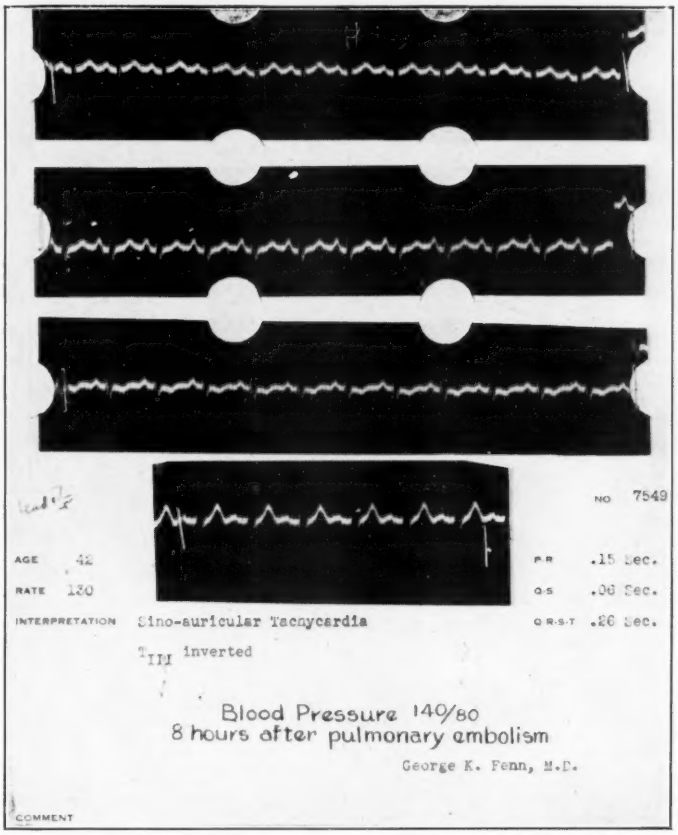

Fig. 8.—Ten days following a lumbar sympathectomy a pulmonary infarct occurred in the right lower lobe. A tracing obtained eight hours after the onset of symptoms revealed an inversion of the T-wave in the third lead. Blood pressure had not fallen but was slightly higher, probably due to pain and anxiety.

nonfatal pulmonary embolism fairly certain. The convalescence of these patients, however, does not resemble the dramatic change in pulse, blood pressure, and color of the patients receiving this medication. In one of our own cases, previously published,[40] the moribund patient was revived within two minutes after the injection of papaverine. Of Denk's nine cases of severe, massive pulmonary embolism, seven showed a dramatic improvement; in the eighth case both pulmonary arteries were completely plugged and in the ninth an embolectomy was the immediate cause of death. Denk advocated the immediate intravenous injection

of two ampules of "eupaverine," cardiac stimulants, and oxygen. A doctor must sit at the bedside of the patient and keep repeating the drug as soon as the pulse gets worse. In Collins' series, ten patients were treated with "spasmalgin" containing pantopon, gr. ⅓ (0.21 gm.); papaverine, gr. ⅙ (0.012 gm.); and "atrinal," gr. 1/60 (0.001 gm.). Nine out of ten cases recovered. Thus, out of a total of twenty patients treated with papaverine, only three died.

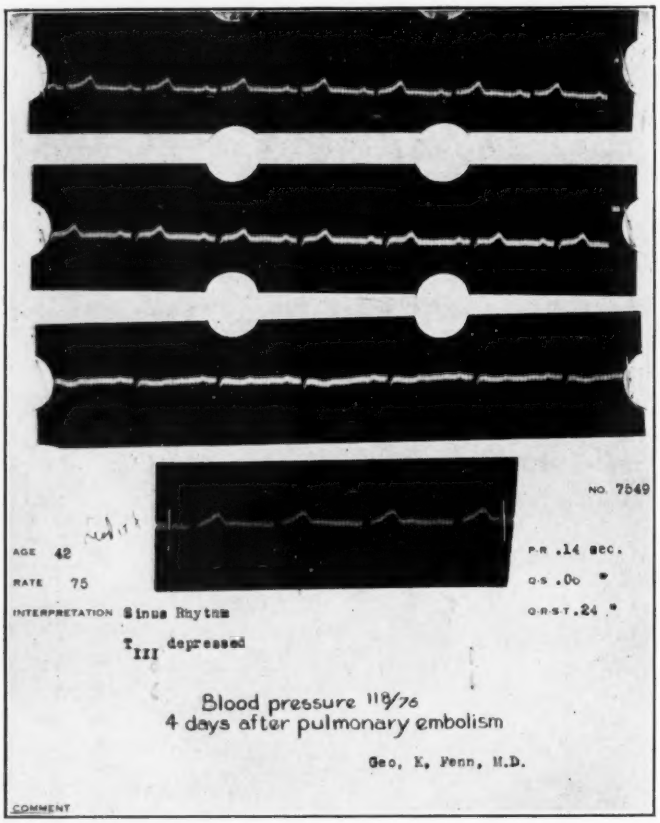

Fig. 9.—Four days after pulmonary embolism T_3 is depressed, but there is some improvement compared with the previous tracing. Blood pressure has returned to the preoperative level.

The use of atropine in pulmonary embolism has been reported by Bardin.[2] Recent evidence of depressor impulses originating from the pulmonary plexus[12-14, 16] and the electrocardiographic changes seen in pulmonary embolism,[9-11, 14] including observations on patients[42, 43] and our own records on animals, might be interpreted as due to vagal stimulation, although the marked fall in systemic blood pressure, occurring in massive pulmonary embolism, may well be responsible for some of the electrocardiographic changes.

Of the clinical material to be discussed elsewhere in detail, we are presenting three cases which have electrocardiographic tracings and illustrate some of the points under discussion. In the case of G. P., electrocardiograms are available before and eight hours, four days, and

twenty-five days after a pulmonary infarct. The first tracing was taken as a routine record before a lumbar sympathectomy for Buerger's disease. There was no history or clinical evidence of cardiac impairment. It will be noted that following the infarct T_3 first became inverted, later depressed, and then again returned to its upright position. Blood pressure readings taken simultaneously with the tracings prove that, at least in this instance, the electrocardiographic changes are not due to a fall in blood pressure (Figs. 7-10).

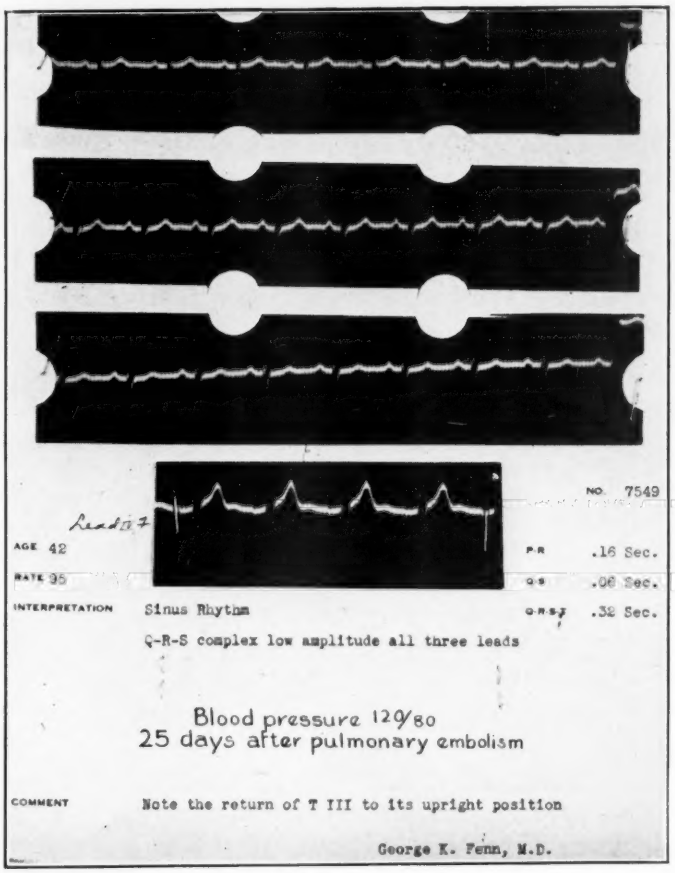

Fig. 10.—Twenty-five days after pulmonary embolism, T_3 returned to its upright position. There is a low amplitude of the QRS complex in all three leads.

In another case of Drs. M. J. Kiley and G. W. Scupham, an electrocardiogram is available twelve hours after a third shower of pulmonary emboli. The blood pressure fell moderately but hardly enough to account for the tracings. While a pre-embolic tracing is not available, an electrocardiogram obtained two and one-half months later shows a disappearance of all the abnormal changes (Figs. 11 and 12).

In a third, fatal case of Drs. H. E. Jones and Arthur A. Elliott, a 65-year-old male patient suddenly collapsed eight days after an appendectomy for a gangrenous appendicitis. Together with dyspnea and cyanosis there was a fall of blood pressure to 30/0, but he recovered

from this attack. The following day, with a blood pressure of 94/72, an electrocardiogram was obtained (Fig. 13). The patient died on the third day following the first syncopal attack. At autopsy multiple obturating emboli of the pulmonary arteries and their small divisions were found, but the main vessel was patent and there was no coronary occlusion.

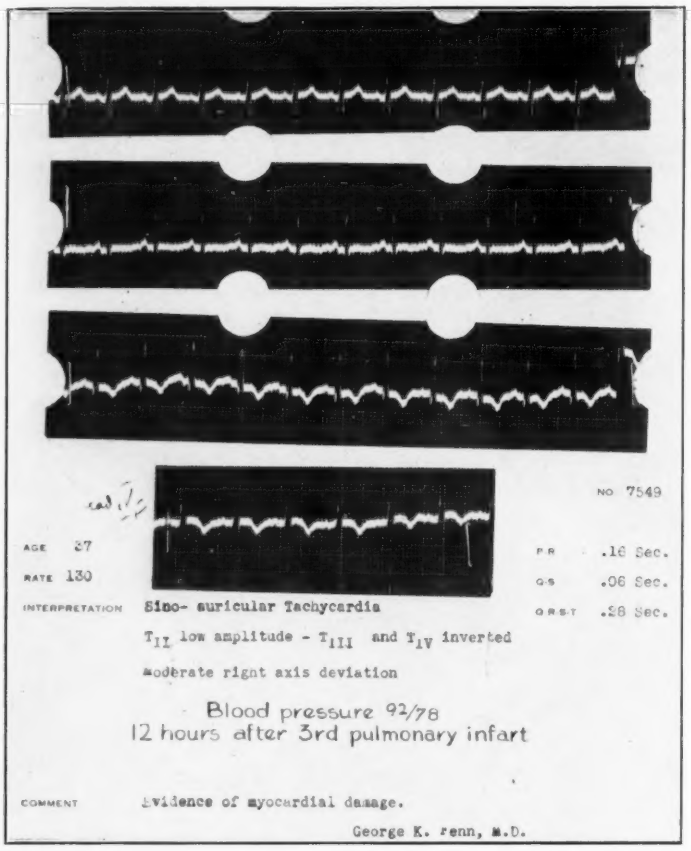

Fig. 11.—This electrocardiogram was obtained twelve hours after a third postoperative pulmonary infarct. Note the low amplitude of T_2, the inversion of T_3 and T_4. There is a moderate right axis deviation. The blood pressure (systolic) fell twenty points.

These three cases illustrate the facts (1) that small or even significant electrocardiographic changes can take place in pulmonary embolism which are reversible; (2) that the fall in blood pressure is not responsible for these changes; (3) that a patient can die of a pulmonary embolus without a massive obstruction; and (4) that the pathologic tracing in the electrocardiogram was not caused by organic coronary occlusion. These changes are either due to right ventricular dilatation and failure, or to reflex vagal effects on the heart, most likely a combination of both.

Whether the electrocardiographic changes are due to vagal coronary constriction or to a reflex vagal depression of the systemic blood pressure,

atropine ought to be useful in inhibiting these reflex changes; while its effect on the vascular tree is negligible, the bronchodilator action may also be of some benefit, thus combating pulmonary edema and atelectasis. A $\frac{1}{150}$ gr. dose of atropine given intravenously is well tolerated; we have given as much as gr. $\frac{1}{60}$ intravenously without any side effect except a transient tachycardia and dryness of the mouth.

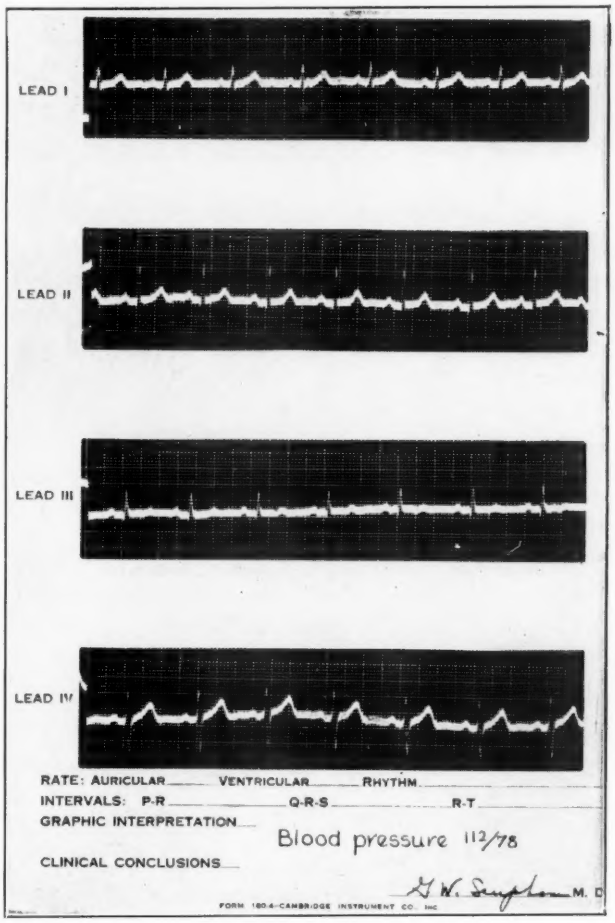

Fig. 12.—Tracing obtained ten weeks later. All the pathologic changes have been reversed.

The use of atropine should not be limited to cases of massive pulmonary embolism which are in extremis but would seem indicated in pulmonary infarcts, where a second or third episode might prove to be fatal. In two recent cases of pulmonary embolism, without cyanosis or shock, the use of atropine, gr. $\frac{1}{150}$, three times a day subcutaneously seemed to improve the dyspnea without, of course, altering the process of consolidation and resolution.*

*Since this article was submitted for publication, experience with the use of atropine and papaverine in the treatment of pulmonary embolism has increased and will be reported in a subsequent publication (Arch. Int. Med.).

The use of oxygen in the form of a tent or by nasal catheter is clearly indicated when dyspnea and cyanosis are present. It was frequently employed in this series and the action on cyanosis and dyspnea often has been marked. In a recently observed case its prompt use greatly relieved the cyanosis; the asphyctic, peripheral type of embolism with no fall in blood pressure but a marked oxygen desaturation, as emphasized by Churchill,[5] is its real field of usefulness.

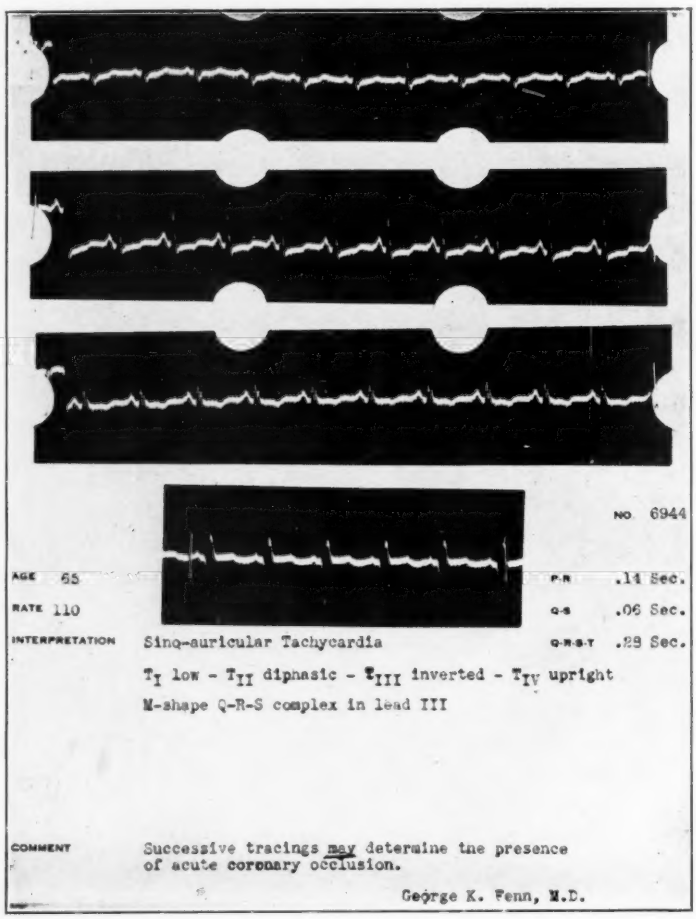

Fig. 13.—Tracing obtained twenty-four hours after a severe, syncopal type of pulmonary embolism. Blood pressure was 94/72. Note that T_1 is low, T_2 diphasic, T_3 inverted, and T_4 upright. There is an M-shaped QRS complex in Lead III. The patient died next day and during his last twenty-four hours two other identical tracings were obtained. At autopsy, multiple peripheral emboli were found, but the main vessel was patent. There was no coronary occlusion and no myocardial lesion.

The use of pressor substances, such as epinephrine, ephedrine, and neosynephrine, is frequently encountered in the histories of patients who exhibit a marked fall in blood pressure. The maintenance of blood pressure is highly desirable to combat cerebral and cardiac ischemia. Epinephrine, however, in our dogs produced such marked pulmonary edema and the rise in pulmonary blood pressure is so definite[26] that it

probably did more harm than good. Ephedrine has been especially recommended by the French authors;[2, 17] its pressor and bronchodilator action may be of benefit. It must be remembered, however, that, as the fall of blood pressure is due to lack of sufficient venous return from the lung to the left heart and an additional reflex vagal action, too much cannot be expected from its use. Neosynephrine, a potent pressor substance, has such a marked stimulating action on the vagus that its use in pulmonary embolism is inadvisable. In a recent study of the use of the drug in spinal anesthesia, Brunner and one of us[27] found that electrocardiographic changes, such as partial heart block and shifting of the pacemaker, can be produced temporarily in normal hearts. One should hesitate to add a vagal stimulant to the vagal hypertonus, which seems to exist in cases of pulmonary embolism.

Digitalis and strophanthin, as advocated by some authors[15] to support the failing right heart, are also strong vagal stimulants; they increase the load on the right heart, do not relieve the increased resistance, and decrease coronary flow.[44]

Venesection, advocated in marked filling of the cervical veins in the absence of shock, cannot help if the right heart is completely exhausted; if it is not, it will promptly build up the same intracardiac pressure as before. The release of some of the peripheral resistance in the pulmonary bed should be the goal of any medical treatment; this is best accomplished by papaverine; whereas, the nitrites, because of their depressant action on systemic blood pressure, are certainly contraindicated.

Recently, the infiltration of the stellate ganglion with procaine has been advocated by Leriche and his co-workers.[45] They studied the postmortem material of the Institute of Pathology at Strasbourg and found that of 225 cases of pulmonary embolism the main trunk or both main branches were obstructed in 159 cases, roughly 70 per cent. That left 30 per cent of the patients who died even though only one branch or one or several lobar arteries were blocked. In this type, the abolition of sympathetic pulmonary vasoconstriction may be life saving in their opinion. Out of three of their personal cases, one was successful but two failed. They advocated having suitable needles on hand in every large ward and infiltrating on the side of the chest pain or bilaterally.

The technique of stellar infiltration is not difficult. We have used it repeatedly in our clinic for a preoperative test before a contemplated sympathectomy. It no doubt releases the sympathetic vasoconstriction of the pulmonary vascular bed, which, according to de Burgh Daly's[7] studies, is quite active. While it is not as simple to carry out as an intravenous injection of papaverine, the suggestion deserves further trial. If it decreases pulmonary hypertension by decreasing the resistance in the pulmonary vascular bed, it may well fit in with our other therapeutic attempts to transform a complete occlusion into a partial one.

DISCUSSION

It is obvious from the start that the massive pulmonary embolus, which plugs the main trunk or both main branches completely, kills instantly or within a few minutes. It is not likely that an embolectomy could be performed soon enough to save such a patient's life. In the statistics quoted by Leriche,[45] 30 per cent of the patients, however, die with the findings of only a comparatively small, partial occlusion. Such cases have been reported several times. As early as 1924, Sauerbruch reported the case of a 32-year-old woman who died from a pulmonary embolism following a hernia operation; an embolus 3 mm. in diameter was found in a small branch of the pulmonary artery, 4 cm. from the periphery of the lung. The major arteries were patent. In our autopsy material a typical death from pulmonary embolism occurred in the presence of minor pulmonary obstruction in seven out of thirty-five cases. Pathologists at present are rather loath to accept such a finding as a cause of death and probably many more such cases will be found in the future.

But if death can occur reflexly from the occlusion of one or two lobar branches, why do patients tolerate a lobectomy or a pneumonectomy without any serious disturbance of circulation? Among others, O'Shaughnessy[46] has studied the reflexes originating from the root of the lung and found respiratory and cardiovascular reflexes originating from the pulmonary plexus which could be abolished by local application of cocaine. Sunder-Plassmann[47] found powerful myelinated nervous receptors in the submucosal bronchial musculature and could obtain cardiac standstill on intrabronchial pressure. He advised topical application of novocain, even during general anesthesia. Cullen and Ravenstone[48] reported three instances in which the patients suddenly died when the hilus of the lung was ligated or cut with the electric cautery. That these events do not occur more frequently is probably due to the depth of anesthesia and the premedication which effectively suppresses such reflexes in the animal experiment. In our own work it was early found that when the animals were under ether anesthesia or under heavy barbiturates the usually fatal dose would not kill them; for this reason only morphine was used as a premedication in all our later work; this drug does not depress vagal reflexes but instead facilitates them.

If one places the pulmonary hypertension proximal to the obstructing clot, as the essential functional lesion contributing to death and responsible for the electrocardiographic changes, then all therapeutic attempts must be focused to relieve this hypertension or to abolish the reflex impulses emanating from it. Papaverine and the infiltration of the stellate ganglion both release the vascular spasm of the arterial tree. This collateral vascular spasm has been repeatedly and unequivocally demonstrated in the peripheral arteries when an embolus plugs the main

arterial pathway.[49] Its demonstration in the pulmonary circulation is difficult, but the work of Daly and his collaborators has adequately shown the potent sympathetic vasoconstriction which operates in the pulmonary vascular tree.

The cause of collapse and the fall in blood pressure usually has been explained by the inadequate transfer of blood from the right heart to the

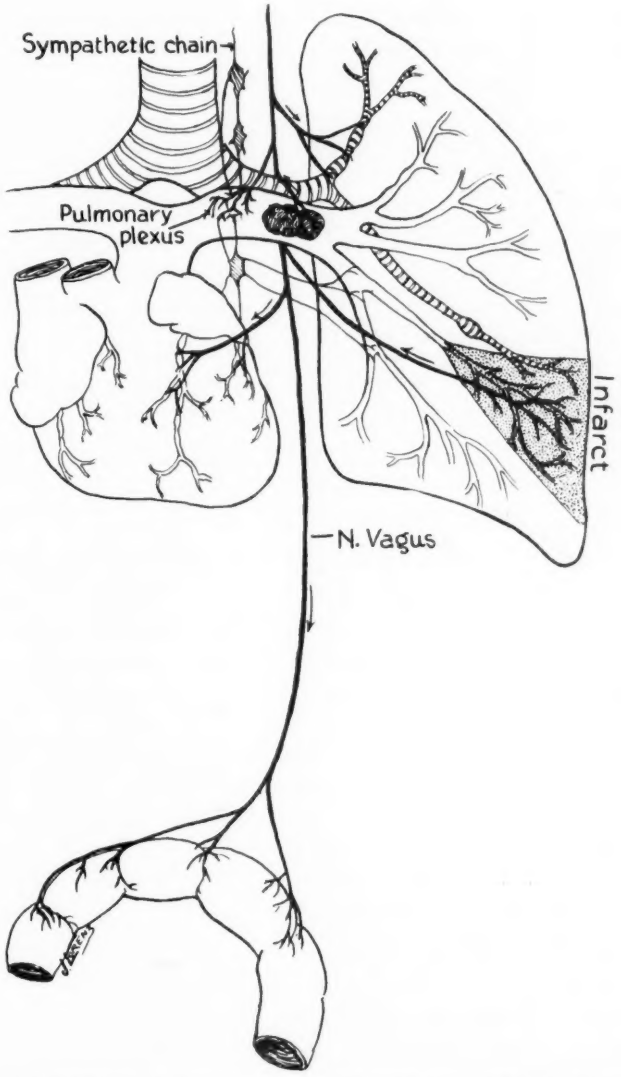

Fig. 14.—The radiation of autonomic reflexes from the occlusion of the pulmonary vascular bed, bronchi, and pleura. The afferent impulses travel mainly in the vagus and radiate back to the lung as bronchoconstrictor and bronchosecretory fibers. They may constrict the coronaries, produce vagal inhibition of the heart, and depress blood pressure. They can radiate to the upper gastrointestinal tract and produce colics, increased and reversed peristalsis. The plug may produce a stimulation of the sympathetic vasoconstrictors or a more general sympathetic stimulation through the dilatation of the right heart (Bainbridge reflex). The hypertension in the right heart and in the pulmonary artery seems to be the main stimulus for these widespread reflexes, although the rise in intrapulmonary pressure, the congested lung, and the irritated pleura all have been shown to act as reflexogenic factors.

left so that effective blood volume is markedly diminished.[5] But we have quoted good evidence for highly sensitized vasoreceptors in and around the pulmonary artery,[12, 13] in the bronchi,[47] and in the pleura,[50] the stimulation of which produces widespread reflex changes, such as fall in blood pressure, vagal inhibition of the heart, coronary constriction, bronchial spasm, and increased gastrointestinal motility (Fig. 14). Some of these reflexes seem to travel through the vagus; their abolition or diminution with atropine seems logical. Thus, while atropine does not affect the pulmonary hypertension, it inhibits a depressor reflex originating from it. This reflex may become a major contributory cause of death.

Oxygen administration seems highly desirable when cyanosis is present or when respiration is labored. There is no need to belabor this point.

Based on this experience, we feel that every surgical floor should be equipped with gr. $\frac{1}{150}$ of atropine tablets and gr. $\frac{1}{2}$ powders of papaverine, both of which can be rapidly boiled in a spoon with a few cubic centimeters of water and injected intravenously; that oxygen tanks should be readily available when a pulmonary infarct has occurred; that the use of digitalis, strophanthin, and neosynephrine in the syncopal type of pulmonary embolism may do more harm than good.

Finally we wish to emphasize again that a large percentage of patients dying from pulmonary embolism will continue to die, in spite of all these measures, when the clot completely obstructs the main artery. Only measures to prevent thrombosis or to prevent the existing thrombosis from breaking loose will diminish the incidence of such fatalities. We wish to draw attention, however, to certain neurocirculatory changes which may turn a nonfatal into a fatal embolus. When surgeons, interns, and nurses are made conscious of certain measures outlined above, this dreaded fatality may be averted in certain favorable cases.

SUMMARY

1. Experimentally, two types of fatal pulmonary embolism have been produced: one which plugs the terminal vascular bed and is characterized by cyanosis and dyspnea; and the other which represents an obstruction to the main pulmonary artery and exhibits a syncopal attack with pallor and fall in blood pressure.

2. The possible mechanisms of death have been analyzed. Atropine protects a large percentage of animals dying from the massive type of embolism, and so does papaverine. Oxygen is helpful in the peripheral type of embolism.

3. Electrocardiograms taken in dogs before and after the production of a massive pulmonary embolism present a picture resembling a serious interference with coronary flow. The possible causes of these findings are analyzed.

4. The clinical application of these findings is discussed. In our series of 100 cases of pulmonary embolism, 87 died and 13 survived. Of the fatal cases, less than 10 per cent died within the first ten minutes, thus allowing time for emergency measures.

5. On the basis of the experimental findings, a combination of atropine and papaverine is advocated to counteract the radiation of autonomic reflexes, which originate in the affected lung. Oxygen is obviously useful in the peripheral type of embolism, in which vasomotor collapse is absent but cyanosis predominates.

6. A few other drugs commonly employed, such as epinephrine, neosynephrine, digitalis, and strophanthin, are discussed but not recommended.

7. As manifest thrombosis of the veins of the pelvis and lower extremities is comparatively rarely encountered in patients with massive pulmonary embolism and heparinization of a large number of postoperative cases is yet impossible, the early and active interference with the described autonomic reflexes occasionally may be the only available life-saving measure.

It is a pleasure to thank Dr. George E. Wakerlin, head of the Department of Physiology, University of Illinois, College of Medicine, for his valuable suggestions and for the use of some of the facilities of his department.

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OVARIAN TUMORS AND UTERINE BLEEDING

I. Granulosa Cell Tumors

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ABNORMAL uterine bleeding may be associated with ovarian tumors. Its diagnostic value in cases of granulosa cell tumor recently has been emphasized. However, the solid granulosa cell tumors comprise only a small group of ovarian neoplasms, 6 out of 100 consecutive cases in Lynch's series, and abnormal menstruation may be associated with other pathologic types. The present study, therefore, was undertaken to determine the relative incidence of uterine bleeding in all varieties of ovarian tumors. The records of 376 ovarian tumors on file in the Surgical Pathological Laboratory of the Johns Hopkins Hospital and the gynecological service of the Church Home and Infirmary were analyzed to determine the types of ovarian neoplasms associated with abnormal bleeding and the pathologic changes responsible for the bleeding. In this study it was found that menstrual irregularities were practically restricted to specific pathologic types of ovarian tumors, but that a variety of mechanisms accounted for the uterine bleeding. The largest group of cases comprises forms of granulosa cell tumor in which the endocrine activity of the tumor (estrogen secretion) results in endometrial hyperplasia and functional bleeding. The second largest group are pseudomucinous cystadenomas (benign and malignant) in which uterine bleeding also may result from endometrial hyperplasia, but in which the underlying endocrine factors are more varied and less accurately understood. The third group comprises papillary cystadenocarcinoma of Müllerian derivation in which abnormal uterine bleeding is the result of tubal or endometrial carcinoma, either metastatic or possibly multicentric in origin. In a fourth group of cases, ovarian neoplasms of teratomatous nature are associated with menstrual disturbances resulting from the endocrine activity of the tumor tissue.

In the present communication the largest group of tumors associated with abnormal uterine bleeding is considered. This comprises the granulosa cell group. A series of 59 typical granulosa cell tumors from the Surgical Pathological Laboratory is reported and in addition a more malignant and papillary form of granulosa cell tumor is described. This form hitherto has not been included and has been loosely grouped as papillary cystadenocarcinoma. Because of the large number of contribu-

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tions to the subject of granulosa cell tumor in the recent literature, the data on the present series of 59 granulosa tumors are briefly summarized and more detailed consideration is given to the papillary granulosa cell carcinoma.

PAPILLARY GRANULOSA CARCINOMA

Among the papillary ovarian carcinomas in the Surgical Pathological Laboratory of the Johns Hopkins Hospital and the Church Home and Infirmary, there are 35 tumors which we believe should be included among the granulosa cell group because of both their morphologic and physiologic properties. This form of ovarian tumor appears in postmenopausal and menopausal women, is frequently associated with abnormal uterine bleeding, and runs a rapidly malignant course; in many cases it has already metastasized when the patient first presents herself for examination. Grossly, the tumor is usually cystic, having sessile papillary projections with a tendency to peritoneal implantations.

This neoplasm has been described and illustrated by Shaw, who groups it with the papillary serous cystadenocarcinomas; and by Varangot, who refers to it as "le végétant épithélioma papillaire atypique." It has been variously referred to in the literature as medullary carcinoma, solid papillary carcinoma, adenocarcinoma and carcinoma in ovarian cyst, but it has never been systematically included in the classification of ovarian tumors.

Approximately 40 per cent of all ovarian carcinomas belong to this group. They can be distinguished from the so-called papillary serous cystadenocarcinoma, or, as we prefer to call it, the Müllerian carcinoma, microscopically, physiologically, and clinically.

Clinical Features.—The tumor characteristically occurs in women who have passed the menopause; 19 out of 27 (72 per cent) cases in which the age is available are postmenopausal. The complaint is usually a gradual increase in the size of the abdomen in association with slight pain. It is significant that 10 out of 22 cases in which menstrual histories were available complained of some form of abnormal uterine bleeding (Table I). A pelvic examination reveals the presence of an irregular or cystic mass in the adnexal region, the malignancy of which may be suspected by the presence of palpable nodules over the surface of the cyst or on the peritoneal coverings in the cul-de-sac. Eleven, or 50 per cent, of our cases in which the location of the tumor is given were either bilateral at the time of operation or later had recurrence in the unaffected ovary. At operation a small amount of bloody ascites may be present and there are frequently peritoneal and omental metastases. The metastases, however, are usually flattened plaques and under the peritoneal serosa rather than the cauliflower, friable transplants of the Müllerian type of papillary tumor (papillary cystadenocarcinoma). Metastases to distant organs and regional lymph nodes occur less commonly.

TABLE I

SUMMARY OF CASE HISTORIES OF PAPILLARY GRANULOSA CARCINOMA

PATH. NO.	AGE	MENSES	INVOLVEMENT	HYPERESTRINISM	THERAPY	RESULTS
18068	46	Regular	Right ovarian cyst, bloody ascites	Tubal hyperplasia	Right salpingo-oophorectomy, x-ray	Died 1 yr., recurrence
18066	49	18 mo. amenorrhea; 6 wk. bleeding	Right ovarian cyst, bloody ascites	-	Right salpingo-oophorectomy, x-ray	Well 1 yr.
10777	44	-	Bilateral ovarian tumors with peritoneal transplants and ascites	Tubal hyperplasia	Bilateral salpingo-oophorectomy	Died 5 mo.
10569	45	Menses 6 days overdue	Bilateral ovarian tumors, peritoneal transplants	-	Hysterectomy, bilateral salpingo-oophorectomy	Died 1½ yr.
9834	53	Menopause 5 yr.; no postmenopausal bleeding	Right ovarian tumor, peritoneal transplants	-	Right salpingo-oophorectomy	-
5885	-	-	-	Tubal hyperplasia	-	-
5711	57	Menopause 7 yr.; no postmenopausal bleeding	Right ovarian tumor	-	Right salpingo-oophorectomy	Died 1 yr., recurrence
5063	-	-	Ovarian cyst	-	-	-
4655	55	Menopause 2 yr.; no postmenopausal bleeding	Bilateral ovarian cysts	Tubal hyperplasia	Bilateral salpingo-oophorectomy	Died 7 mo., recurrence
3792	58	Menopause at 38 yr. of age; bloody spotting, 3 wk.	Pelvic mass	-	-	-
2247	50	Menopause at 41 yr. of age; vaginal bleeding, 2 days 3 mo. ago	Bilateral ovarian tumors, peritoneal metastasis	-	Bilateral salpingo-oophorectomy	-

1590	59	Menopause 7 yr.; vaginal bleeding, 1 yr.	Bilateral ovarian cysts, peritoneal metastasis	Endometrial hyperplasia	Panhysterectomy with bilateral salpingo-oophorectomy	-
12289	53	-	-	-	-	Death 1 yr.
17728	50	Menopause at 44 yr. of age	Left ovarian tumor, ascites	-	-	-
18143	-	-	-	-	-	-
20274	58	Menopause at 55 yr. of age	Right ovarian tumor	Hyperplasia of tube	Right salpingo-oophorectomy	Died
20300	-	-	-	-	-	-
28919	56	-	Bilateral ovarian tumors, peritoneal metastasis	-	Bilateral salpingo-oophorectomy	Died postoperatively
30942	45	Flooding 2½ yr.	Bilateral ovarian tumors	Endometrial hyperplasia	Hysterectomy, bilateral salpingo-oophorectomy	Alive 8 yr.
34424	-	-	-	-	-	-
40210	49	Regular until operation 5 mo. ago	Bilateral ovarian masses	-	Left salpingo-oophorectomy; right ovary previously removed	Died 5 mo., recurrence
46926	40	Regular	-	-	-	Died 11 mo.
48816	40	Regular	-	-	-	-
49512	36	-	-	-	-	-
54604	68	Menopause 20 yr. ago	Generalized abdominal metastasis	-	-	Died 6 wk.
55424	64	Menopause at 52 yr. of age; 2 mo. bleeding	Right ovarian cyst	Endometrial hyperplasia	-	-

TABLE I—CONT'D

PATH. NO.	AGE	MENSES	INVOLVEMENT	HYPERESTRINISM	THERAPY	RESULT
57458	50	Menopause at 48 yr. of age	Right multilocular ovarian cyst, peritoneal metastasis	-	Hysterectomy, right salpingo-oophorectomy	Died postoperatively
57466	50	Menopause at 49 yr. of age; spotting 10 days	Right ovarian cyst	-	Right salpingo-oophorectomy	Death 13 mo., recurrence and metastasis
57562	50	Menopause at 48 yr. of age; no postmenopausal bleeding	Ovarian cyst with lymphatic, peritoneal, and omental involvement	-	Removal of tumor	Death 8 mo.
57526	30	Menorrhagia and dysmenorrhea 1 yr.	Right ovarian cyst, bloody ascites	-	-	-
57740	67	Menopause 12 yr. ago; no postmenopausal bleeding	Right ovarian cyst	-	-	-
57742	42	Regular	-	-	Right salpingo-oophorectomy; x-ray	Death 27 mo.
58288	61	No postmenopausal bleeding	-	-	-	-
58434	-	-	Widespread abdominal metastasis	-	-	-
59144	52	Menopause at 50 yr. of age; spotting on three occasions	Right ovarian cyst	-	-	-

Pathology.—Grossly the tumor is polycystic with papillary portions. These papillary areas, however, are usually flattened and resemble mulberries rather than the grapelike projections of the Müllerian tumor. The cysts, which are usually unilocular, reach an average size of 12 cm.

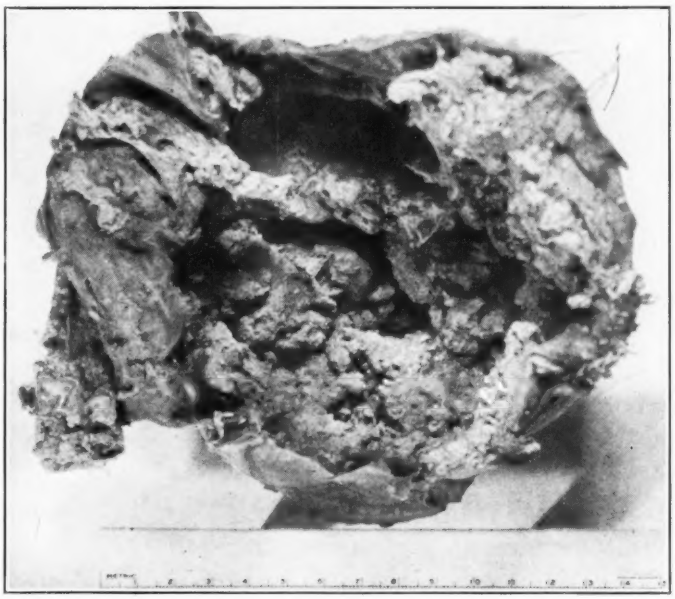

Fig. 1.—Path. No. 30942. Gross specimen of papillary granulosa cell carcinoma, showing cyst filled with finely papillary growth.

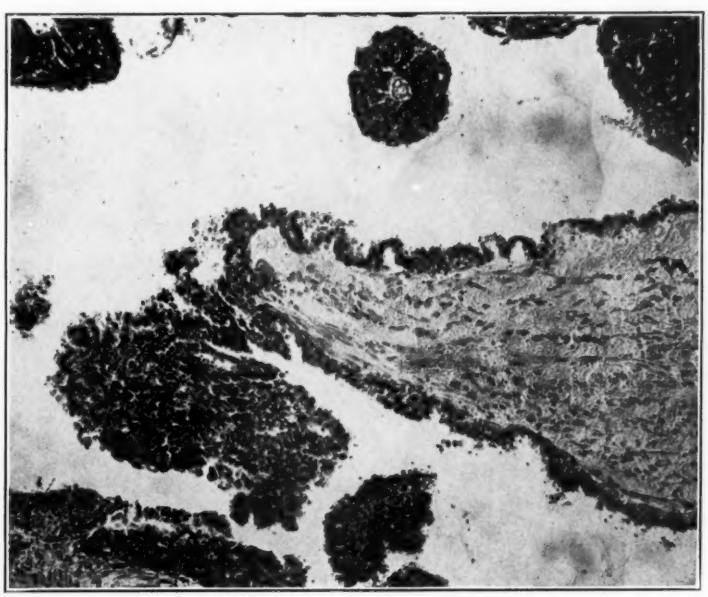

Fig. 2.—Path. No. 28919. Papillary type of granulosa cell carcinoma showing cyst lined with many layers of granulosa like cells and typical cross section of a papillary projection.

in diameter but may attain even larger dimensions. The largest tumor in the present series measured 21 by 8 by 5 cm. The content of the cysts differs greatly, grading from a bloody, viscid, gelatinous material to a thin, serous, yellow fluid. The appearance of such cysts in granu-

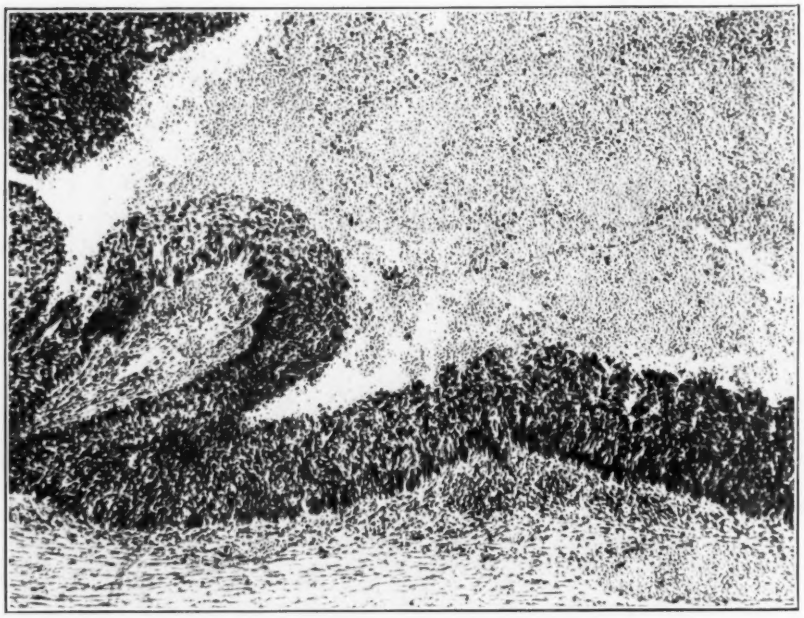

Fig. 3.—Path. No. 40210. Epidermoid border of a cyst in a papillary granulosa cell carcinoma, showing thecalike reaction of underlying stroma.

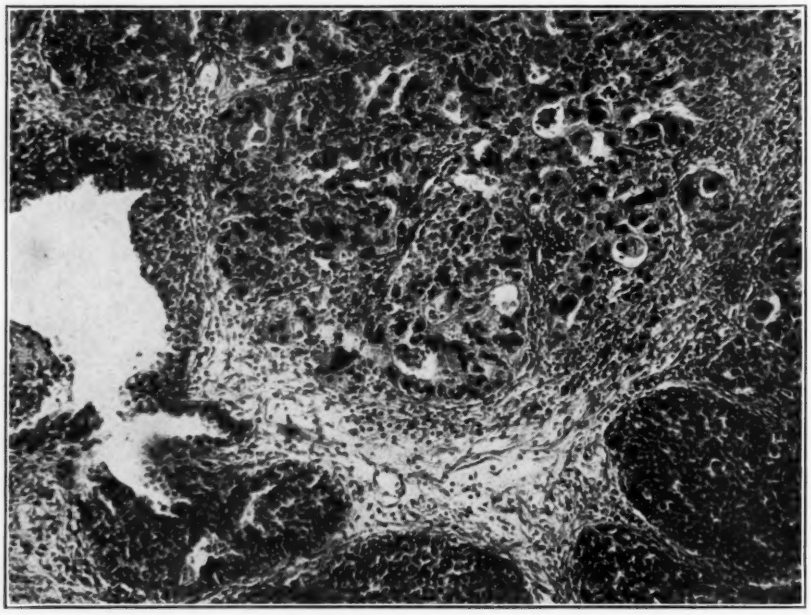

Fig. 4.—Path. No. 58288. Illustrating the variation in size of cells in certain areas of a papillary granulosa cell carcinoma.

losa cell tumors is not unusual; indeed, it is not uncommon for them to reach 8 or 10 cm. in diameter as mentioned below under the gross description of the micro- and macrofollicular types of granulosa cell tumor. The solid tumor tissue is usually yellow in color and of brainlike consistency. Its cut surface is cellular and can be teased apart to show a fine, papillary structure (Fig. 1). These solid portions may completely occlude the cyst. Two cases of the present series were described as solid tumors.

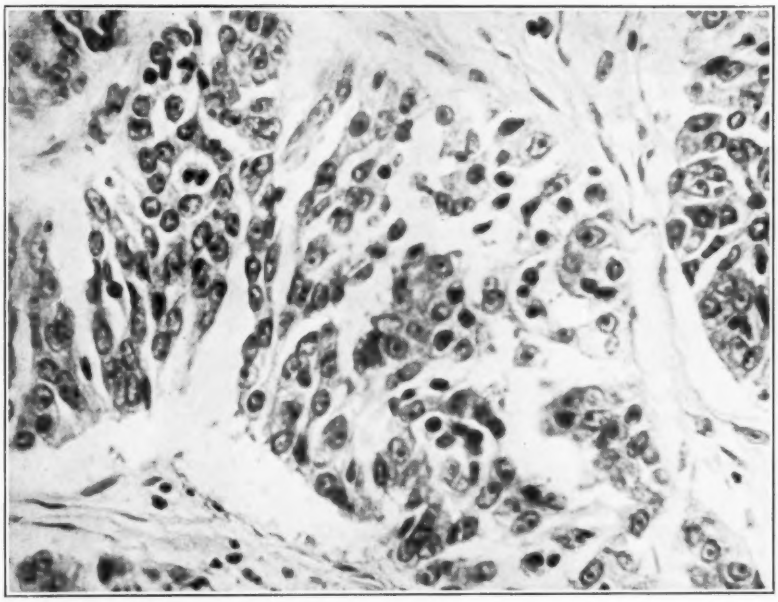

Fig. 5.—Path. No. 18066. A perpendicular arrangement of cells bordering a cyst seen occasionally in the papillary granulosa cell carcinoma.

Microscopically the tumor is characterized by broad, flat layers of epidermoid cells from three to twenty-five rows deep, lining cysts in a pseudopapillary arrangement (Fig. 2). Occasionally there are cysts lined by a single row of atypical cuboidal cells. A cross section of the papillary projections shows a centrally placed blood vessel surrounded by the typical band of epidermoid cells (Fig. 2). Some of the epidermoid borders have well-defined basement membranes, while others merge into the underlying stroma (Fig. 3). In some areas the abundant stroma is invaded by solid islands of the epidermoid cells. Mitotic figures are frequent and there is a great variation in the staining and size of the cells, which in places attain diameters of 15 mm. (Fig. 4). Still other areas present cysts which appear to be lined by perpendicular columns of the same epithelial cells. There are spaces between these columns which resemble superficially Call-Exner bodies (Fig. 5).

Follow-Up Reports.—The tumor is extremely malignant as the operative findings frequently indicate. Of 18 followed cases, 15 were

dead in less than three years postoperatively. Two are still living less than two years postoperatively and only 1 is living over five years. In this case small bilateral ovarian tumors were found unexpectedly during an operation performed for uterine bleeding. A bilateral salpingo-oophorectomy and hysterectomy were performed.

Treatment.—Because the tumors exhibit a marked tendency to occur bilaterally, bilateral salpingo-oophorectomy and hysterectomy were the operations of choice. A hysterectomy is advised if the condition of the patient permits, first, because the uterus is a useless organ after a bilateral salpingo-oophorectomy has been performed; and second, because of the possibility of its involvement in the malignant process. In cases associated with uterine bleeding, either the uterus should be removed at operation or a dilatation and curettage should be performed preoperatively to eliminate the possibility of secondary transplants or concomitant tumors in the uterus.

A study of 9 cases in which a unilateral salpingo-oophorectomy was performed, showed 4 cases with proved recurrences in the remaining ovary from three to eighteen months postoperatively. As most of the patients are approaching or have already passed the menopause, 19 out of 27 cases, the interference with biologic function is usually not an important consideration. This is in sharp contrast to the more benign forms of granulosa cell tumors which occurred during active sexual life in 62 per cent of the cases (Table III). In 231 cases of solid granulosa cell tumors collected from the literature by Varangot, 134 cases occurred in women during active sexual life in contrast to 97 at or near the menopause. An attempt should be made to establish the pathologic diagnosis at the time of operation and in doubtful cases a frozen section should be obtained.

Irradiation therapy was limited to 4 cases, 1 of which was treated elsewhere and the details of treatment are unknown. However, in this case the tumor was incompletely removed as implants were already present at the time of operation. A bilateral salpingo-oophorectomy and hysterectomy were performed and deep x-ray therapy was administered postoperatively. The patient died one and one-half years postoperatively. The results obtained in the other three cases were also poor (Table II). Two completely operable cases were given prophylactic postoperative irradiation. One is dead from a massive recurrence and the other, although still alive one and one-half years postoperatively, has a mass in the opposite ovary which is probably a recurrent carcinoma. A case in which the tumor was incompletely removed at operation was relieved of ascites for a short while, but there was never a noticeable decrease in the size of the abdominal mass.

Pathologic Physiology and Histogenesis.—The clinical histories of the reported cases give certain clues as to their histogenesis as has previously been suggested. Ten out of 22 cases, or 45 per cent, complained of either

TABLE II

TABLE OF IRRADIATION THERAPY IN PAPILLARY GRANULOSA CARCINOMA

CASE NO.	OPERABILITY	OPERATION	X-RAY THERAPY	RADIUM THERAPY	RESULTS
18068	Operable	Right salpingo-oophorectomy 1/26/37 Exploratory 1/24/38	Prophylactic 3/1-8/37, 9,500 r.*; 10/2-12/3, 2,000 r.	12/30/37-1/14/38 Total, 16.6 gm. hr.†	Recurrence 5/22/37 Death 1/24/38 with massive recurrence
18066	Operable	Right salpingo-oophorectomy 1/26/37	Prophylactic 2/16-27/37, 8,000 r.*; 4/5/37 1,000 r.	None	8/20/38 cystic mass in left adnexal area, probably recurrence
10596	Partially operable	Bilateral salpingo-oophorectomy and hysterectomy 1/30/30	4/11-14/30, 2,500 r.‡	8 gm. hr., 1/27/31§ 4/11-13/31, 10 gm. hr.¶	2/27/31 mass unchanged, no ascites; 4/11/31 recurrent ascites; 8/31/31 death

*Factors: Filter, 1 mm. Cu, 1 mm. Al, 30 Ma., 210 KVP, 50 F.S.D., time 4 min., 8 portals 10/10 cm.

†Factors: Emanations used, 4 abdominal portals, time 1 hr., 2,667 to 4,110 mc., filter 2 inch platinum at 2 inch distance.

‡Factors: Filter 1 mm. Cu, 1 mm. Al, 30 Ma., 200 KVP, 50 F.S.D., time 20 min., 5 portals 20/20 cm.

§Factors: Emanations used, 4 abdominal portals, time 30 min., 2,890 to 3,638 mc., plain pack at 2 inch distance.

¶Factors: Emanations used, 2 abdominal portals, time 1 hr., 3,228 to 3,506 mc., 2 inch cylinder at 3 inch distance.

profuse menstruation or postmenopausal bleeding. Although this cannot be accepted as absolute evidence of hyperestrinism, it is certainly suggestive when other lesions have been excluded as a cause of bleeding. In a series of 59 solid granulosa cell tumors tabulated below, 62 per cent complained of abnormal menses. In contrast to these findings, not a single case in a series of papillary ovarian carcinoma of Müllerian type was associated with abnormal uterine bleeding unless there was an associated uterine or tubal growth.

Endometrium was available in only three cases and in all it was hyperplastic. A study of the tubal epithelium in five cases showed definite hyperplasia in four and active epithelium in one postmenopausal case. Such histologic findings are comparable to those found in a study of uterine and tubal mucosa in a series of cases in which a typical granulosa cell tumor was present. It therefore seems that patients with papillary carcinoma of the above-described type are bleeding because of the effects of endocrine stimulation on the endometrium. Since this is also the cause of bleeding in patients with typical granulosa cell tumors, the histologic findings may be used as presumptive evidence that the papillary ovarian carcinoma under discussion belongs to the granulosa cell group.

Morphologically the cells of the papillary carcinoma described are similar to those of the diffuse and microfollicular forms of granulosa tumor and bear a greater resemblance to the true granulosa cells than

TABLE III

SUMMARY OF CASE HISTORIES OF SOLID GRANULOSA CELL TUMORS

CHARACTER	PATH NO.	AGE	MENSES	INVOLVEMENT	TREATMENT	RESULT
Diffuse with dermoid cyst	57720	39	9 mo. amenorrhea	Right ovarian cyst	Right salpingo-oophorectomy	Living 9 mo. postoperatively
Diffuse	16213	13	Irregular	Left ovary; ascites	Left salpingo-oophorectomy	Living 16 yr.
	21701		Irregular; hyperplasia	----------	Bilateral salpingo-oophorectomy, hysterectomy	Dead ?
	28216	56	Operative menopause	Left ovary	Left salpingo-oophorectomy	----------
	29820	49	Irregular; hyperplasia	Ascites	X-ray, hysterectomy, bilateral salpingo-oophorectomy	----------
	37276	64	----------	Operations 1922 and 1925	----------	Well 3 yr.
	40452	13	Normal	----------	----------	Well 8 yr.
	49712	47	Hysterectomy	Bilateral with peritoneal metastasis	Bilateral salpingo-oophorectomy	Well 2 yr.
	53984	25	----------	----------	----------	Died at 30 days with widespread metastasis
	55358	59	Postmenopausal bleeding	Omental metastasis	Laparotomy	----------
	57464	32	----------	Left ovarian tumor	----------	Died with lung metastasis and local recurrence
	57532	73	----------	----------	----------	----------
	57554	48	Irregular	Unilateral	Oophorectomy	Living 4 yr.
	57560	54	No postmenopausal bleeding	----------	----------	----------

	57636	16	Amenorrhea 2 mo.; negative Friedman test	----------	Ascites	Living 2 mo.
	57866	51	----------	Left cyst	Hysterectomy, left salpingo-oophorectomy	----------
	57980	53	----------	Liver and intestines	----------	----------
	59096	54	----------	----------	----------	----------
Sarcomatous	36790	64	Leucorrhea	Left ovary	Hysterectomy, bilateral salpingo-oophorectomy	Died 11 yr. postoperatively
	52214	42	Regular	----------	----------	Living, 2 mo.
	52498	56	Vaginal bleeding	Solid ovarian tumor removed 1½ yr. previously	Laparotomy?	Died 1 yr.
	53986	25	----------	----------	----------	Well 18 mo.
	54150	62	No postmenopausal bleeding	----------	----------	Died postoperatively
	56236	65	No postmenopausal bleeding	----------	----------	----------
	57572	22	Amenorrhea 2 mo.; negative Friedman test	Right ovarian tumor	Operation, x-ray	Died 2½ yr., metastasis to liver and lungs
	57884	45	Regular	----------	----------	----------
	58302	--	----------	----------	----------	----------
	58580	21	Amenorrhea 2 mo.	----------	----------	3 mo. axillary nodes
	59142	33	Prolonged and profuse	Left side	Hysterectomy, bilateral salpingo-oophorectomy	----------
	61055	--	----------	----------	----------	----------
	C.H.I. 19076	31	Irregular 1 yr.; amenorrhea 3 yr.	Right ovarian cyst; myoma	Right salpingo-oophorectomy; myomectomy	Living and well 9 mo. postoperatively

TABLE III—CONT'D

CHARACTER	PATH. NO.	AGE	MENSES	INVOLVEMENT	TREATMENT	RESULT
Microfollicular	35234	31	----------	One side removed and recurred in operation 2 mo. later	----------	----------
	36966	59	Brownish discharge; hyperthyroidism	----------	----------	----------
	51196	44	Regular; amenorrhea 2 yr.	Left ovarian cyst	----------	Died postoperatively
	57442	53	Irregular 6 mo.; hyperplasia	Unilateral	Hysterectomy, bilateral salpingo-oophorectomy	----------
	57744	42	Amenorrhea 8 mo. with occasional spotting; positive Friedman test	Left ovarian cyst; peritoneal metastasis	Operation, x-ray treatment	Died 15 mo. postoperatively
	57990	--	----------	----------	----------	----------
	58260	26	Irregular; endometrial hyperplasia	----------	----------	----------
	58836	43	Irregular; hyperplasia	Unilateral	Hysterectomy, unilateral salpingo-oophorectomy	----------
	59132	43	----------	Left intraligamentary cyst	Hysterectomy, left salpingo-oophorectomy	Living and well 7 yr. postoperatively
	(Church Home and Infirmary)	48	10 mo. amenorrhea; 8 mo. bleeding; hyperplasia	Left ovarian cyst	Bilateral salpingo-oophorectomy panhysterectomy	Living 18 yr. postoperatively
	----	22	Always irregular and profuse	----------	----------	----------
Cylindroid	4948	--	----------	----------	----------	----------
	13364	3	----------	Bilateral	----------	Died 6 mo., widespread metastasis

	15850	--	----------	----------	----------	----------
	24407	44	Regular; recurrence ē bleeding; hyperplasia	Left ovary, 1919; recurrence at site, 1935	Left salpingo-oophorectomy, 1919; removal of tumor; right salpingo-oophorectomy; hysterectomy, 1935	Recurrence 16 yr. postoperatively
	34126	48	Irregular	----------	----------	----------
	36180	43	----------	Right ovarian cyst ruptured	----------	----------
	41094	--	----------	----------	----------	----------
	57530	21	Regular	Right ovary	Right salpingo-oophorectomy	Recurrence and died 2 yr. postoperatively
	59136	59	Postmenopausal bleeding	Right ovarian cyst, intraligamentary	Supravaginal hysterectomy	Living and well 4 yr. 3 mo.
	2032 (Church Home and Infirmary)	39	Amenorrhea 2 mo.	Bilateral ovarian tumors	Right intraligamentary cyst Bilateral salpingo-oophorectomy	Died 3 mo. postoperatively
Lipidique	40518	35	Regular	Left ovarian cyst	----------	Living and well 8½ yr.
	57640	37	Regular	Right ovarian cyst; peritoneal and omental metastases	----------	Died 1 mo.
	57870	55	Postmenopausal bleeding	Right solid tumor; left cyst	Hysterectomy; bilateral salpingo-oophorectomy	----------
	59128	46	----------	Unilateral cyst; peritoneal metastasis	Salpingo-oophorectomy	Died 1 mo., cerebral metastasis
	59140	37	Irregular	Left ovarian tumor	----------	----------
Tubular	57644	55	Regular, hysterectomy	Ascites	Laparotomy	Died without operation
	59130	50	Brownish discharge; menopause 2 yr. ago	Right tumor with abdominal metastasis	Laparotomy operation	Died 2 mo. postoperatively

some of the other subdivisions of the granulosa class. Certain areas of the papillary tumors under discussion show more variations in nuclear size and staining characteristics and a greater number of mitotic figures than previously described for the forms of granulosa cell tumors. However, this is in keeping with their more malignant character. The tumor is therefore to be regarded histologically as the most malignant type of granulosa cell tumor and the source itself of the estrin responsible for the endometrial hyperplasia.

SOLID GRANULOSA CELL TUMORS

All of the recognized types of solid granulosa cell tumors have been briefly reviewed and clinical data on 59 cases recorded in the Surgical Pathological Laboratory have been tabulated.

Granulosa cell tumors have been much discussed during the past decade and it is well recognized that clinically the cases present a hyperestrin syndrome consisting of abnormal uterine bleeding and engorged painful breasts. The menstrual irregularities are typically those produced by endometrial hyperplasia, that is, intervals of amenorrhea of two to six months' duration succeeded by long periods of menorrhagia; dysmenorrhea is never present. This syndrome is so striking when it appears after the climacteric that these cases have been over-emphasized and the impression is frequently gained that granulosa cell tumors occur more commonly in postmenopausal women. Such an impression is erroneous since 28, or 61 per cent, of the cases in the present series occurred before the age of 50 years. Seventy-five per cent of the cases collected by Varangot occurred during active menstrual life. (Table III.)

Sixty-two per cent of the cases complained of abnormal uterine bleeding. Endometrium was available in only 7 cases in the present series and in every instance endometrial hyperplasia was found. There were 2 cases with myomata uteri.

The malignancy of granulosa cell tumors is given by Varangot as 25 per cent, excluding postoperative deaths. Of 146 cases collected from the literature, 20 died postoperatively, 32 had metastasis and recurrences, 63 were living and well under five years, and 28 were living and well over five years. In the series reported by Novak and Brawner, 28 per cent of the cases were malignant. In our series of 32 followed cases, 15 are dead, 11 are living and well under five years, and 7 are well over five years. In all, 46 per cent were malignant. Because of the tendency to late recurrence and metastasis, the prognosis should be guarded. In one case in the present series a recurrence took place sixteen years following the original operation (Case, Path. No. 24407, reported by Compton[1]).

The radiosensitivity of the granulosa cell tumor is difficult to evaluate because of the paucity of records available and because of the relatively

benign course in some cases. Two patients in the present series treated by x-ray died within three years. In one case (Path. No. 57744) no data as to the amount of therapy given were available. In the second case (Path. No. 57572) the patient received 1,856 roentgen units to each of four portals, 10 by 10, two anterior and two posterior, over a period of three weeks. The factors used were 30 Ma., 210 KVP, at 50 S.T.D. with 1 mm. Cu 1 mm. Al filter for ten minutes. The patient had had peritoneal transplants at operation and therefore should be classified as a partially operable case. She responded well for one and one-half years. A recurrent pelvic tumor was then palpated; an exploratory laparotomy was performed and the condition was found to be inoperable. A second intensive course in x-ray therapy was inaugurated, but the mass continued to grow rapidly and the patient died with liver and lung metastases two and one-half years after the primary operation. In five cases from the literature which were treated as fibroids because of a mistaken diagnosis, castration doses of x-ray failed to produce any change in the size of the tumor or a decrease in the uterine bleeding (cases of Schulze, Wolfe and Kaminester, Opitz, and von Szathmary, all quoted by Varangot).

Although the granulosa cell tumors present a uniform clinical syndrome, they do not represent a single pathologic entity. The first pathologic classification of the granulosa cell tumors was given by Meyer in his monograph of 1915. He divided the group into four subdivisions: (1) the macro- and microfollicular, (2) the diffuse, (3) the cylindroid, and (4) the sarcomatous. Since the appearance of Meyer's publication, authors almost universally have accepted his classification with the addition of two further subdivisions, "the folliculoma lipidique," sometimes referred to as the luteinized granulosa cell tumor; and the tubular granulosa cell tumor. The "fibroma theca cellulare xanthomatoides" of Löffler and Priesel has not been included as we consider that this tumor belongs to the sarcomatous group of Meyer.

The Micro- and Macrofollicular.—This type of granulosa cell tumor is one of the most easily recognized varieties as it bears the closest resemblance to the Graafian follicle. It is composed of small cells arranged concentrically about cystic spaces which frequently contain an eosin-staining substance. These folliculoid structures may be micro- or macroscopic in size. Call-Exner bodies are sometimes present. The connective tissue stroma, which is fairly abundant, shows an increased cellularity about the basement membrane of the follicles. The cells themselves have large nuclei and proportionately little cytoplasm. In places they seem to merge into the epithelioid cells of the folliculoid structures showing a striking resemblance to the cells of the theca interna (Fig. 6).

Grossly this tumor may appear to be completely solid, but more frequently it contains cysts which may vary from a few millimeters to over 10 cm. in diameter. On section the solid portions are composed

of cellular tissue of brainlike consistency which is yellow or sometimes even reddish in color. The cystic cavities may contain a coagulated gelatin-like material or a bloody serous fluid.

The Diffuse.—The diffuse type of granulosa cell tumor is similar to the micro- and macrofollicular type grossly. Microscopically it is characterized by solid insular areas of small cells which are roughly polyhedral in shape and have pale hematoxylin-staining nuclei with very little cytoplasm. There is a heavy connective tissue stroma surrounding these islands. The stroma is very acellular and hyalinization is occasionally seen. (Fig. 7.)

The Cylindroid.—This variety of tumor is composed of closely packed columns of small cells resembling those of the diffuse type. These columns are arranged in intricate patterns by a fine connective tissue network. (Fig. 8.)

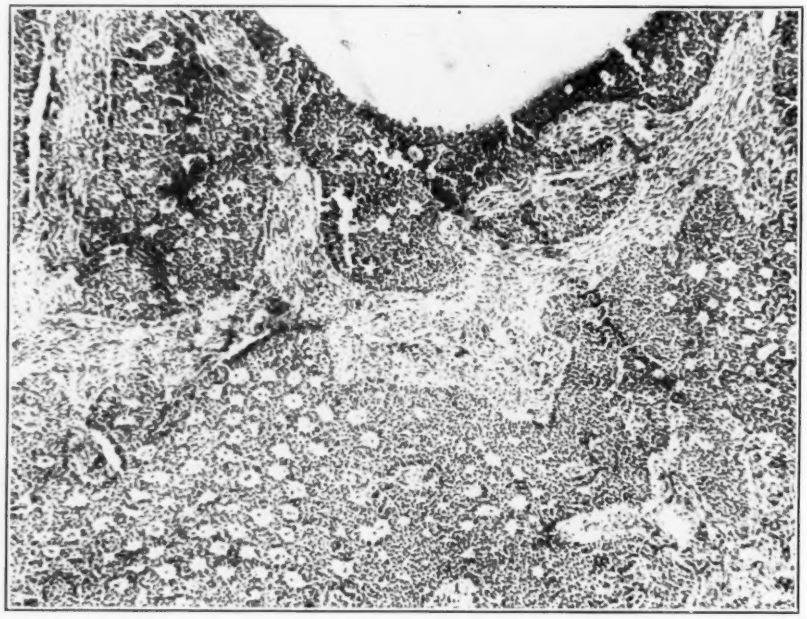

Fig. 6.—Path. No. 58260. Microfollicular type of granulosa cell tumor, showing the lining of one small cyst and a more solid portion of the tumor with many Call-Exner bodies. The cell type resembles that seen in Fig. 3.

The Sarcomatous.—The sarcomatous type of granulosa cell tumor is the most difficult to recognize as it represents the most undifferentiated form. Grossly it is a solid tumor which resembles a fibroma of the ovary and on section shows a glistening white fibrous surface flecked with a yellow lipoid material. Microscopically the cells are spindle in shape and arranged in whorls giving the watered silk appearance characteristic of connective tissue tumors. Giant cells, however, are rare, thus distinguishing them from true connective tissue sarcomas of the ovary. The tumor is cellular and toward the periphery a tendency to form minute follicles may be seen. Cholesterin crystals are frequently

present. This form is frequently confused with fibroma of the ovary and indeed the association with hyperestrinism is sometimes the only means of establishing a correct differential diagnosis. (Fig. 9.)

The cells of the sarcomatous granulosa cell tumor are apparently closely related to the theca cells and, therefore, the tumor has been described as a theca cell tumor. However, because its embryonic origin from the mesenchyme, its production of estrin, and its prognosis and treatment all are identical with those of the granulosa cell tumor, we prefer not to make a separate classification of such tumors.

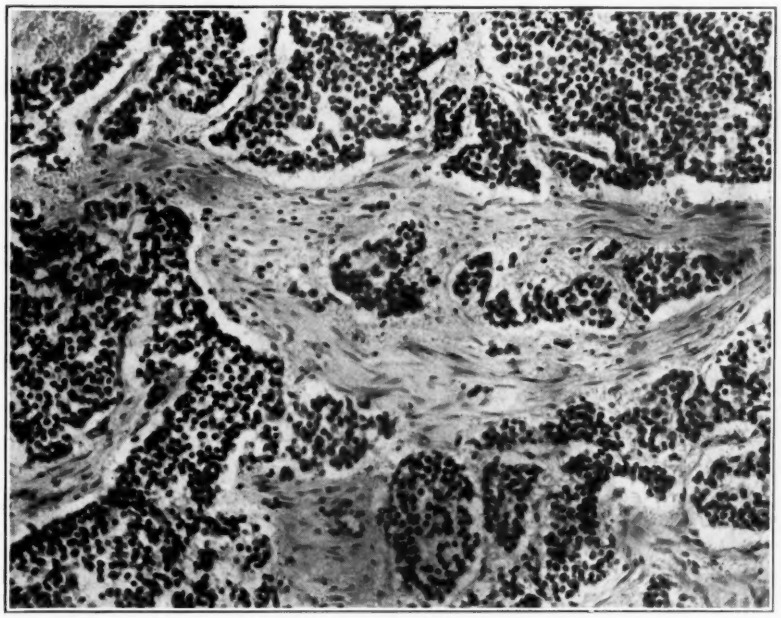

Fig. 7.—Path. No. 57980. Diffuse type, showing insular area of granulosa cells surrounded by a dense connective tissue stroma. The cell type resembles that seen in the more insular areas of Fig. 10.

The Tubular Type.—This form of granulosa cell tumor is extremely rare. It was recognized by Meyer and referred to as a granulosa cell tumor with unusual tubular areas. Microscopically it is composed of many small tubules of cuboidal cells with a clearly defined basement membrane and a secretory edge. The lumen of these small glands may or may not be filled with an eosin-staining material. There may be associated areas of solid tumor cells and also macrofollicular zones. (Fig. 10.) It is important not to confuse this type of tumor with the tubular testicular adenoma of Pick or more undifferentiated forms of arrhenoblastoma.

Varangot has described a case of this type in his monograph on granulosa cell tumors. His case was also clinically and physiologically a granulosa cell tumor.

The Folliculoma Lipidique.—The sixth type of granulosa cell tumor is also extremely rare, only three cases having been reported in the

literature. It was first described by Marion in 1910. Lecéne reviewed Marion's case and reported an additional case in 1927 (published by Moulonguet and Dobkevitch in 1931) and in 1933 Plate reported a third case.

The tumor is characterized grossly by a yellow color. Microscopically it resembles the diffuse type of granulosa cell tumor except for the

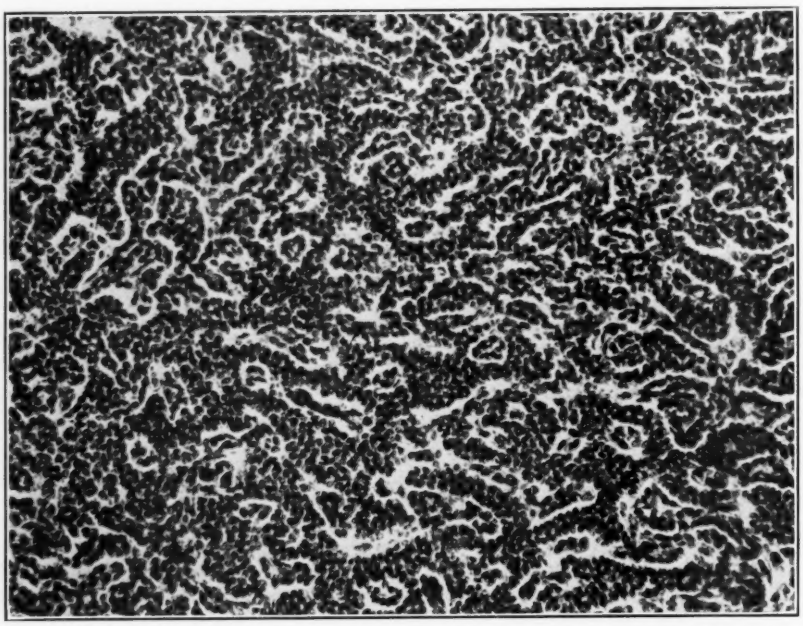

Fig. 8.—Path. No. 59136. Typical pattern of cylindroid granulosa cell tumor.

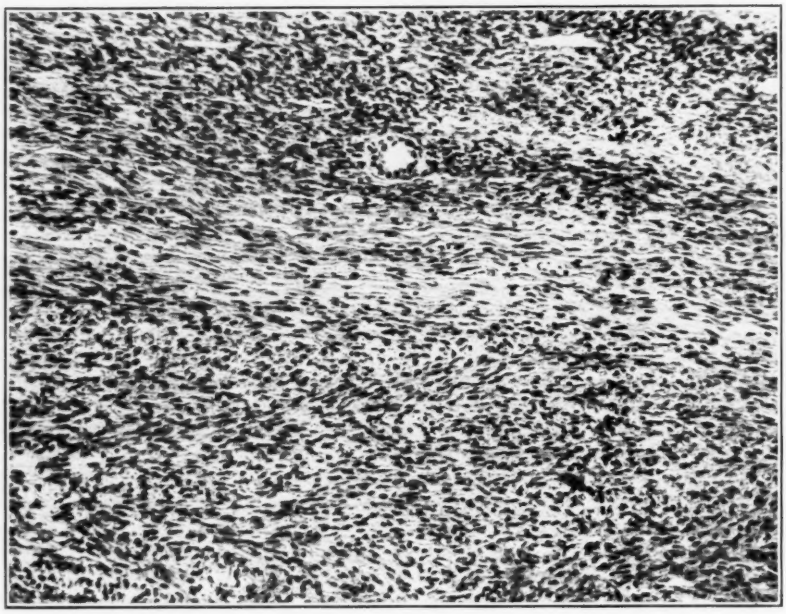

Fig. 9.—Path. No. 59143. Small follicle surrounded by spindle cells of a sarcomatous granulosa cell tumor.

abundance of lipoid material crowding each cell. This gives the tumor cells a certain resemblance to lutein cells and also to those of adrenal rest tumors. (Fig. 11.) Indeed, both Lecéne and Plate regarded it as a luteinized granulosa cell tumor; however, Varangot, who gives an excellent review of the subject, on the basis of physiologic evidence refuses to consider the tumor as such. The endometrium in Lecéne's

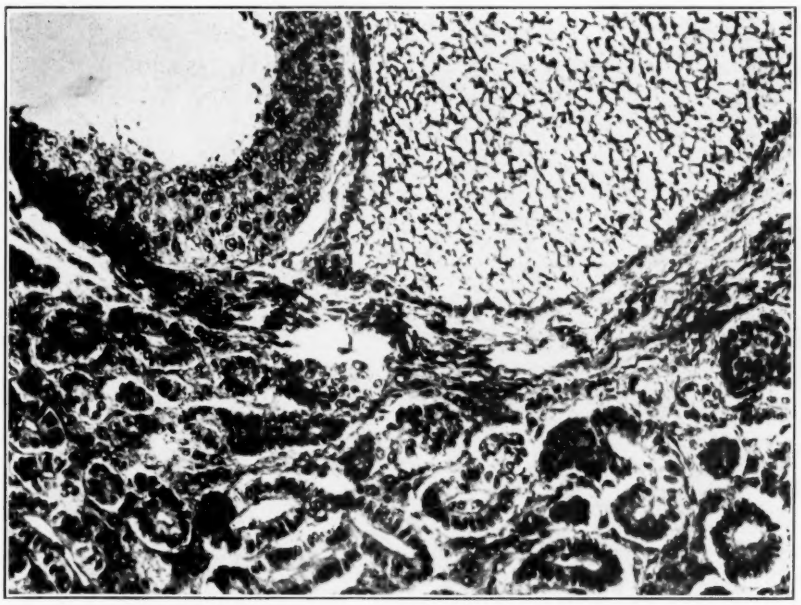

Fig. 10.—Path. No. 59686. Illustrating a tubular granulosa cell tumor having a microfollicular area.

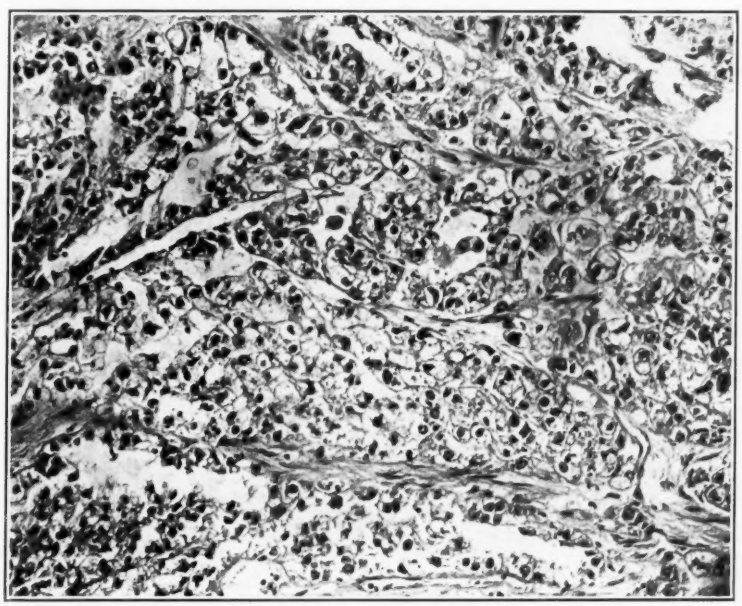

Fig. 11.—Path. No. 57870. Folliculoma lipidique showing abundant intracellular lipoid material.

cases showed hyperplasia and no secretory activity. Plate reports that the endometrium of his case was "très hyperplasique" with no further qualification. Therefore, physiologically the tumors can be classified as granulosa in origin, but cannot be considered as luteinized.

SUMMARY

Abnormal uterine bleeding in association with ovarian tumors has been analyzed as to cause and frequency in a group of 376 cases from the Surgical Pathological Laboratory of the Johns Hopkins Hospital and the Gynecological Service of the Church Home and Infirmary and the cases have been studied according to their pathologic classification. It has been found that abnormalities in menstruation occur among a variety of pathologic types of ovarian tumors but that the mechanism responsible for these abnormalities varies with the tumor type.

The highest occurrence of abnormal uterine bleeding was found in association with the tumors of granulosa derivation. It is this group which has been considered in the present paper. A group of 35 cases heretofore included under the classification of papillary serous cystadenocarcinoma has been added to the granulosa cell tumors as papillary granulosa cell carcinoma on the basis of morphologic and clinical characteristics. In 35 cases reviewed, 45 per cent were associated with abnormal uterine bleeding. A group of 59 solid granulosa cell tumors has been reviewed according to the pathologic type and 62 per cent were found to be associated with menstrual abnormalities. In both groups where endometrium was available, endometrial hyperplasia was the direct cause of the uterine bleeding. The hyperplasia is presumably produced by the estrogenic secretion of the tumor itself.

A more careful study of the uterine endometrium, together with hormonal studies on the blood and urine of patients with ovarian neoplasms, will render valuable assistance in the correct classification of ovarian tumors.

The authors wish to express their appreciation for the assistance and advice of Dr. Charles F. Geschickter and Dr. Vernon H. Norwood which have made this study possible.

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CYSTADENOMA OF THE OVARY INCORPORATED BETWEEN THE LEAVES OF THE MESOSIGMOID

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THE technical difficulties of removal are not great in the majority of instances of cystadenoma of the ovary. Adhesions to surrounding parietes, particularly to the intestines, are the most frequent causes of difficult surgical removal. In a review of 658 oophorectomies done for cystic and solid tumors, Spencer[1] found adhesions present in 448 (68 per cent).

So-called intraligamentary cysts developing between the leaves of the broad ligament were encountered in approximately 1 per cent of a series of 1,063 cases of ovarian tumor reported by Bernstein.[2] Considering the retroperitoneal origin of the ovary in close relationship with the mesonephros or embryonic kidney and its descent into the pelvis, where it becomes encased in its own mesentery, it is rather remarkable that the intraligamentary position is not more frequently encountered. This is borne out by the classical work of Dowd,[3] who, in 1900, reported a case in which a cystic tumor had developed between the leaves of the transverse mesocolon. Microscopic examination of the cyst wall revealed its structure to be identical with that of ovarian cystadenoma, while chemical examination of its fluid contents indicated it to be strikingly similar to that found in ovarian cysts. Considering these points of similarity, together with the anatomical approximation of the root of the mesentery and the retroperitoneal origin of the ovary, Dowd expounded the theory that such mesenteric cysts develop from ovarian tissue sequestrated from the main ovarian mass during its descent into the pelvis during embryonic life. He believed that mesenteric dermoid cysts probably arise from similarly sequestrated ovarian tissue and pointed out that such sequestration is not infrequently encountered in other organs, notably the thyroid and spleen. He further recognized that mesenteric cysts whose walls have a microscopic structure similar to that of the intestine are probably a result of sequestration into the mesentery from the intestine. Dowd's views on the origin of mesenteric cysts have been widely accepted by present-day writers.[4-8]

Mesenteric cysts most frequently develop in the mesentery of the lower ileum, but they may occur in the mesentery of any part of the gastrointestinal tract, including the mesosigmoid. Conceding the correctness

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of Dowd's theory that many mesenteric cysts arise from sequestrations from the ovary, we find reported in the literature a considerable number of such cysts in the mesentery of the sigmoid[9, 10] although this is said to be the least common site.[11] For practical purposes such cysts are not and should not be classified as ovarian cysts. Herewith is reported a case in which a true cystadenoma of the left ovary developed between the leaves of the mesosigmoid. Report of a similar case has not been found in an extensive review of the literature.

CASE REPORT

The patient, a married woman, 30 years of age, was admitted to the Framingham Union Hospital on March 12, 1938, complaining of lower abdominal pain of two years' duration.

The past history is significant in that in 1915, at the age of 7½ years, she was treated at another hospital for pelvic abscess. At this time she gave a history of right lower quadrant abdominal pain of forty-eight hours' duration associated with nausea and vomiting. Marked tenderness was present in the right lower quadrant, with a white blood count of 17,600. Because of the presence of a rather marked acidosis, it was felt that her condition did not warrant immediate operation. She was therefore treated conservatively for twelve days, during which time her condition improved and her temperature, which reached a maximum of 105° F. at the beginning of her hospitalization, fell practically to normal. During this period she developed a tender mass in the lower abdomen which appeared to arise from the pelvis. The most prominent portion of the mass lay slightly to the left of the midline. She was operated upon through a lower midline incision. An abscess cavity was opened with the discharge of thick, odorless pus. The abscess was found to have several ramifications among the coils of small intestine, the main one reaching deeply into the pelvis on the left side and the other going superficially toward the region of the bladder in the median line. No mention was made in the hospital record as to the etiology of the abscess. The appendix was not removed, and the condition of the internal genitals was not noted. Following an uneventful postoperative convalescence, she was discharged from the hospital. When seen in the out-patient department of the same institution eight months later, her general health was noted to be good. There was a small hernia in the middle third of the operative scar.

Following this episode the patient enjoyed excellent health until the onset of her present illness. Her physical development was apparently normal. Menarche occurred at the age of 13 years. Menstrual periods have always been irregular varying from five to seven weeks with a rather scanty flow persisting for three days.

Two years ago, following an uneventful pregnancy, she was delivered of a normal male child. Following delivery she first noted the presence of a dull, dragging abdominal pain which was intermittent and definitely worse at the time of her menstrual periods. This discomfort progressively increased in severity. Three weeks before admission the patient fell against the corner of a table striking the lower abdomen in the region of the left lower quadrant. Following this she first noted a swelling of the lower abdomen and was conscious of a sensation of pressure in the lower abdomen and pelvis. She had one normal menstrual period following this episode. The patient had always been constipated, though this had been worse during the six months prior to admission. She also complained of hemorrhoids during this interval.

Physical examination at the time of admission to the hospital revealed a well-developed and well-nourished woman, 30 years of age, who appeared to be in excellent health. A lower midline scar three and one-half inches in length was well healed except in the middle third where a separation of the fascia admitted the tip of the index finger. In the lower abdomen a mass approximately six inches in diameter could be felt extending from a little to the right of the midline well into the left lower quadrant. The mass appeared to be arising from the pelvis and extended upward to the level of the umbilicus. It was smoothly spherical in outline, nontender, and of a semifluctuant consistency which gave the impression that it was definitely cystic in character.

On bimanual examination the mass could be felt to arise from the left side of the pelvis. The fundus of the uterus could be definitely palpated, was of normal size and consistency and in an anterior position, although pushed somewhat to the right by the tumor mass. The latter was slightly movable in all directions, but it could not be moved freely in any direction. The right adnexa appeared to be entirely normal.

Fig. 1.—Barium enema study showing the upper half of the sigmoid colon displaced by an ovarian cyst which has developed between the leaves of the mesosigmoid. The distal half of the sigmoid lies coiled upon itself in the depth of the pelvis.

Barium enema studies (Fig. 1) revealed that the upper portion of the sigmoid was displaced upward and to the right by a rounded mass which extended upward from the true pelvis. The lower half of the sigmoid colon lay folded upon itself in the depths of the pelvis behind the tumor mass. The tumor appeared to be arising from outside the colon and caused no obstruction to its lumen.

Laboratory examination showed the urine to be normal. A mild hypochromic anemia was present with a red cell count of 3,900,000 and a hemoglobin content of 9.8 gm. per 100 c.c. The white cell count was 7,600 with a normal differential cell count. A slight achromia of the red cells was noted.

A preoperative diagnosis was made of cystadenoma of the left ovary with adhesions to the surrounding pelvic structures and to the sigmoid colon. Operation

was performed on March 5, 1938, through a midline incision extending from the symphysis pubis upward to the left of the umbilicus. The scar of the previous operation was excised. In the center of the scar was a small hernia through which a bit of omentum protruded. When the peritoneal cavity was opened, a cystic mass approximately six inches in diameter was found to extend from the brim of the true pelvis upward two-thirds of the distance to the umbilicus. The upper half of the sigmoid colon was adherent to the circumference of the cyst throughout all but its posterior quadrant (Fig. 2). Swinging the cyst and the attached sigmoid laterally revealed that the cyst was contained between the leaves of the mesosigmoid. Tough fibrous adhesions firmly bound the fundus of the uterus to the dome of the bladder.

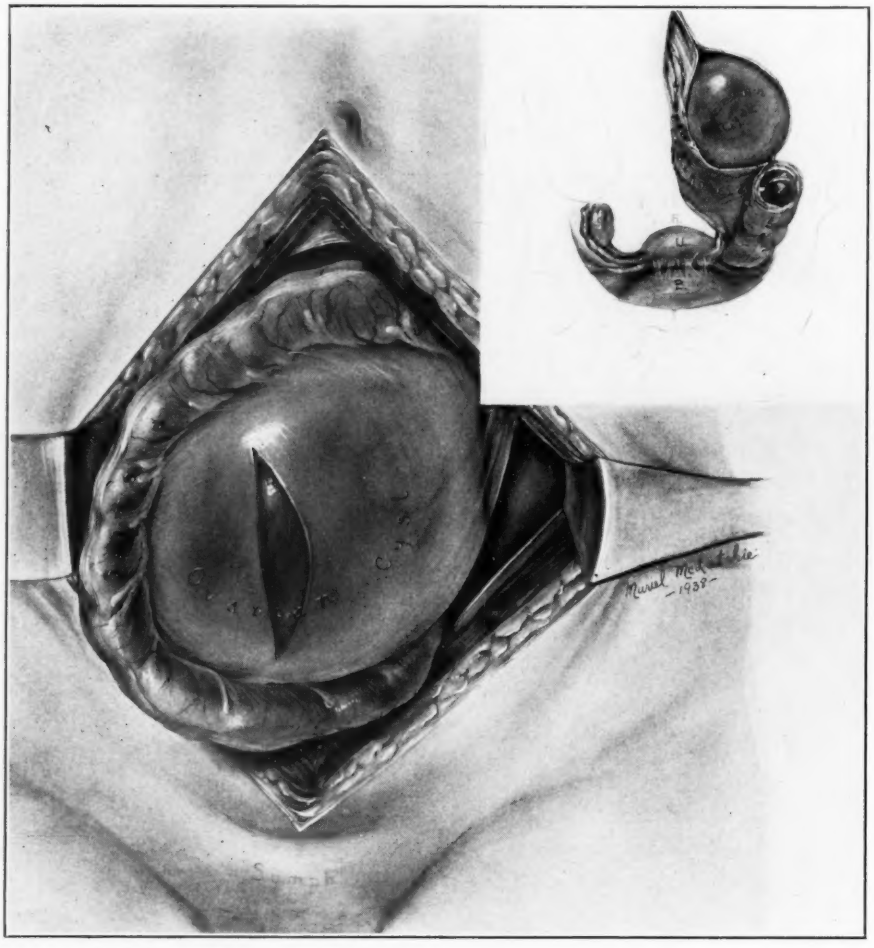

Fig. 2.—Incision in lateral leaf of mesosigmoid through which ovarian cyst was removed. Inset shows relation of structures involved.

The round ligament on the left side followed its normal course anterior to the bowel. From its point of insertion into the horn of the uterus, the left uterine tube proceeded posterior to the bowel and, along with the poorly-defined ovarian ligament, pierced the medial leaf of the mesosigmoid (inset Fig. 2) at a point about one-half inch from the uterus. The remainder of the tube, very much stretched and thinned out, was seen to course over the medial and anterior quadrants of the cyst beneath the medial leaf of the mesentery of the sigmoid (Fig. 3). The sigmoid

vessels lay between the medial leaf of the mesosigmoid and the wall of the cyst, the lateral leaf being relatively avascular.

The lateral leaf of the mesosigmoid was divided in a transverse direction and the plane of cleavage established between the peritoneum and the wall of the cyst. By means of blunt dissection, the wall of the cyst was completely freed both medially and laterally. Firm adhesions between the two layers made it necessary to use sharp dissection in many places, but the freeing-up process was eventually accomplished without injury to the sigmoidal vessels. The ovarian vessels descended retroperitoneally and entered the cyst in its posterior superior quadrant. They were doubly ligated and divided.

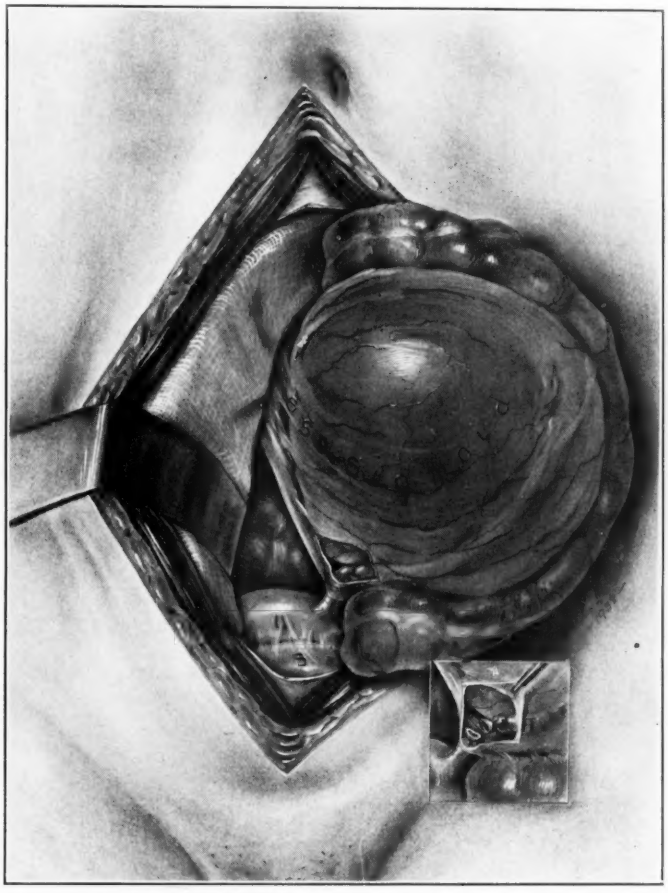

Fig. 3.—Medial relations of cyst. Note tube piercing medial leaf of mesosigmoid. Inset shows division of tube through a small incision in medial leaf of mesosigmoid.

After the cyst had been entirely freed, a small incision was made in the medial leaf of the mesosigmoid, just above the entrance of the tube. The tube and ovarian ligament were ligated and divided (inset Fig. 3) through this incision, and the cyst was removed through the incision in the lateral leaf. After careful hemostasis had been secured, the incisions in the two leaves of the mesosigmoid were sutured with catgut. The right tube and ovary appeared to be entirely normal and were not disturbed. The appendix was found to lie free in the right iliac fossa and was shorter and thicker than is usual with an irregular tip which suggested that a portion of the appendix had sloughed off during the childhood episode alluded to above.

The appendix was removed in the usual fashion and the abdominal wound was closed in layers without drainage.

The postoperative convalescence was entirely uneventful, the temperature never exceeding 100° F. and remaining normal after the third postoperative day. At no time did the patient exhibit symptoms or signs of ileus. The wound healed by first intention, and the patient was discharged from the hospital on the seventeenth postoperative day.

When seen six months after discharge from the hospital, she was feeling well and doing her housework without discomfort. Menstrual periods had been normal, the

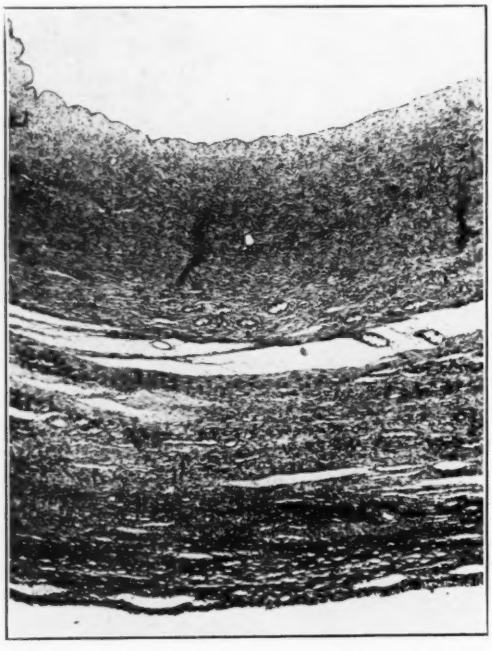

Fig. 4.—Photomicrograph of cyst wall showing lining of squamous epithelium.

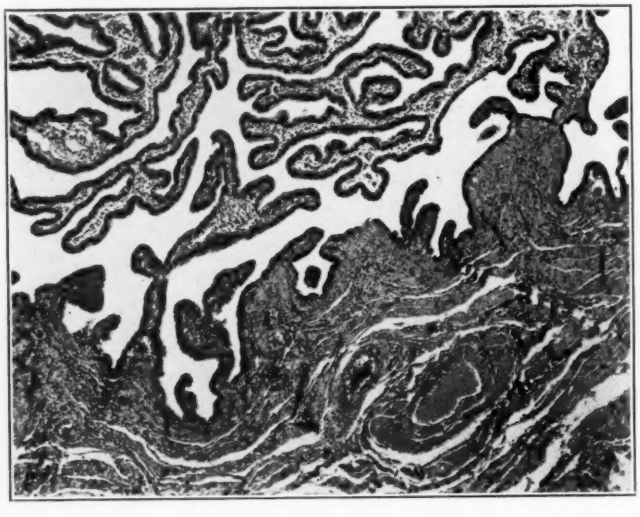

Fig. 5.—Photomicrograph of Fallopian tube, showing absence of pathology in this structure.

bowels had been regular without catharsis, and the lower abdominal discomfort had entirely disappeared.

Dr. S. B. Thorson, who examined the surgical specimen, reported: "The specimen consists of a cyst which has been previously opened and which measures 8 by 6 by 6 cm. In the wall of the cyst ovarian tissue is recognizable. The inner surface is smooth and reveals no papillary structures. A Fallopian tube measuring 9 by 0.7 cm. is present revealing numerous fibrous adhesions near the surface. The lumen is patent and reveals no exudate or fibrous adhesions. This tube extends along the wall of the cyst and finally is incorporated in it.

"Microscopic examination of the cyst wall [Fig. 4] shows it to be lined by a layer of flattened epithelium surrounded by what appears to be functioning ovarian tissue. Examination of sections through the Fallopian tube [Fig. 5] reveals no evidence of pathology in this structure.

"Microscopically the appendix shows evidence of an old, healed appendicitis with partial obliteration of its lumen. In addition there is slight, acute periappendicitis present."

DISCUSSION

That displaced ovarian tissue tends to undergo cystic degeneration is attested by the numerous published reports of cases of ovarian cyst developing between the leaves of the broad ligaments.[12-14] How the ovary becomes misplaced to a position between the leaves of the broad ligament is a matter about which little comment is made in the literature. In speaking of dermoids of the ovary Graves[15] states: "The majority of the tumors are well pedunculated and follow in their growth the usual path of migration (of the ovary) in the abdomen. Occasionally they may be intraligamentary, presumably when the point of origin was close to the hilum of the ovary." This may be the route whereby other types of cystic disease of the ovary assume an intraligamentary position. On the other hand, because of its retroperitoneal origin, it would seem logical to assume that in certain instances the ovary remains in a position between the leaves of the ligaments because formation of the mesovarium fails to take place or is incomplete. No data relative to this point have been found.

Because of the close anatomical association between the origins of the left broad ligament and the mesosigmoid from the parietal peritoneum, it is not difficult to imagine how a progressively enlarging intraligamentary cyst of the left ovary might dissect the peritoneum from the posterior abdominal wall in a lateral direction and finally come to assume a position between the leaves of the mesosigmoid.

In studying the anatomical relationships of the origins of the left infundibulopelvic ligament and the mesosigmoid, Cova[16] found that the origins of the two were separated from each other by a distance of 2 to 3 cm. in 46 per cent of cases. In 15 per cent of cases the mesosigmoid and left infundibulopelvic ligament were found in contact with each other at their origin from the parietal peritoneum, while in 39 per cent the two formed at their origin a single peritoneal fold. It is in the latter group of cases that an enlarging intraligamentary left ovarian

cyst could most easily find its way to a position between the leaves of the mesosigmoid.

In speaking of intraligamentary ovarian cysts Berkeley and Bonney[17] state that: "If the cyst starts between the ovarian and uterine vessels it forces its way upward until the ovarian vessels and Fallopian tube lie sessile on its upper surface and in close relation with each other.

"At a later stage the tumor grows backwards, progressively stripping the peritoneum and ureter from off the lateral pelvic wall so that the posterior layer of the broad ligament is gradually displaced toward the opposite side and in time the pouch of Douglas is entirely obliterated. When this happens, adhesion occurs between the contiguous peritoneal surfaces covering the cyst, the back of the uterus and the opposite broad ligament. During this process the cyst makes its way between the layers of the mesosigmoid and underneath the peritoneal covering of the rectum, until the bowel comes to lie sessile on its upper and inner surface."

It is altogether possible that the cystadenoma in the case herewith described dissected its way to a position between the leaves of the mesosigmoid in a manner similar to that described above. However, at operation the left tube and ovarian ligament appeared to perforate the medial leaf of the mesosigmoid. In view of the history of a pelvic abscess in childhood with a definite ramification to the left side of the pelvis, it seems more logical to assume that this abscess (or the surgery required for its drainage) in some manner injured the medial leaf and forced a herniation of the tube and ovary into a position between the leaves of the mesosigmoid. Because of its abnormal position, cystic degeneration followed. When the clinical history of the childhood illness and the present gross and microscopic findings are considered, it seems probable that appendicitis with perforation was responsible for the pelvic abscess.

SUMMARY

1. A case of cystadenoma of the left ovary lying between the leaves of the mesentery of the sigmoid colon is presented. In a fairly complete review of the literature, a similar case has not been found.

2. A pelvic abscess sustained in childhood is probably responsible for the unusual location of this cyst.

3. The origin of mesenteric cysts and of intraligamentary ovarian cysts is briefly discussed.

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A SIMPLE, EFFICIENT METHOD TO DIMINISH THE INCIDENCE OF PRIMARY AND SECONDARY INFECTION IN SURGICAL WOUNDS*

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ALL surgeons should be aroused to a renewed interest in the subject of infection of clinical wounds through the recent publication, among others, of the following papers: (1) "Sterilization of the Air in the Operative Region With Bactericidal Radiant Energy," by Hart and Gardner;[2] (2) "The Study of Wound Healing," by Reid;[6] (3) "Is Adequate Masking Essential for the Patient's Protection?" by Davis;[1] (4) "The Surgical Principles Involved in the Treatment of Open Injuries," by Mason;[4] and (5) "The Bacterial Flora of Clean Surgical Wounds," by Ives and Hirshfeld.[3]

From the scientific experiments of these workers, it is unequivocally apparent that, aside from all other long-recognized potential factors of infection of clinical wounds, such as contact infection from defectively sterilized hands, gloves, instruments, skin in the field of operation, sutures, ligatures, dressings, faulty hemostasis, rough handling of tissues, mass ligature necrosis, excessive bulk of catgut in ligatures and sutures, suturing which interferes with proper blood supply, use of strong antiseptic solutions with resulting necrosis or diminished functional repair ability of cells, there actually exists today in every operating room a most potent source of direct infection, one which strikes with a frequency and viciousness directly related to the following factors:

1. The number of human beings present in the operating room.
2. The frequency with which the room is used.
3. The time of year, the highest incidence of such clinical wound infections being coincident with high rate respiratory infections of humans.
4. That there are nearly always in the room carriers of *Staphylococcus aureus* or the hemolytic streptococcus.
5. That the surgeon, himself, unwittingly may be the carrier.
6. That it is practically impossible to guard against droplet infections without the use of impossible face and nose masks.
7. That practically all operating rooms contain, in the air and on the floors, walls, and ceilings, more staphylococci and, at times, hemo-

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lytic streptococci than any other department in the hospital except the Nose and Throat Department.

8. That *Staphylococcus aureus* is the principal and general source of infection of clinical wounds.

9. That these infecting agents gain direct entrance to the wound by precipitation from the air overlying the wound and by droplet infection.

10. That every wound made by the surgeon is contaminated and potentially infected in direct proportion to its size and the length of time of its exposure.

11. That a run of such cases always means that the air of the room contains, as proved by culture, a higher percentage of these organisms than normally.

12. That the percentage of viable bacteria reaching the wound may be greatly diminished, almost to the vanishing point, through appropriate continuous special ultraviolet radiation of the air and field of operation, with a resultant marked percentage reduction in the incidence of infected wounds.

13. That while the average incidence of such baleful clinical wound infections is from 4 to 6 per cent (heretofore recognized as an irreducible minimum) it at times rises to 18 to 20 per cent.

14. That a scientific bacteriologic checkup on every link in the so-called aseptic chain may achieve a 100 per cent credit, and yet the incidence of clinical wound infections continue at two to three times the average.

The work of Mason at the Northwestern University Medical School emphasizes the fact that it is within the power of the surgeon to change a contaminated, traumatic wound into a surgically purified one which generally will heal per primam without the use of any antiseptic whatever, provided soap may be so classified.

Inasmuch as every operative wound is contaminated and potentially infected, why should we not cleanse it in the same way?

Some to whom the idea was mentioned disparaged it as being an entirely unnecessary procedure, messy, and unsurgical, and stated it would soften the catgut, devitalize the cells, and violate the present great surgical principle of keeping the wound as dry as possible. However, it seemed entirely logical to conclude that, if contaminated, traumatic wounds with bruised, ragged, lacerated tissues containing grease and visible dirt by painstaking, careful débridement and thorough mechanical soap cleansing could be routinely transformed into wounds which would heal, in the great majority of instances, without infection; then surely the same cleansing process should be even more efficacious in nonlacerated wounds made by the surgeon which likewise, as proved, are always contaminated.

Our problem presented two outstanding questions.

1. Will the same thorough cleansing with soap and water used in accidental wounds militate in any way against ideal healing if applied to clinical surgical wounds before closing them?

2. In a clinical wound proved by culture to be contaminated, what percentage of success in debacterialization may be expected by cleansing with soap and water?

1. However clean and aseptic an operating room appears, wound infecting organisms are always present in the air and on the walls.

A simple metal Petri dish support was devised to hang from a light bracket in the field of operation (Fig. 1). At three separate morning surgical clinics, blood agar Petri dish exposures were made for three hours.

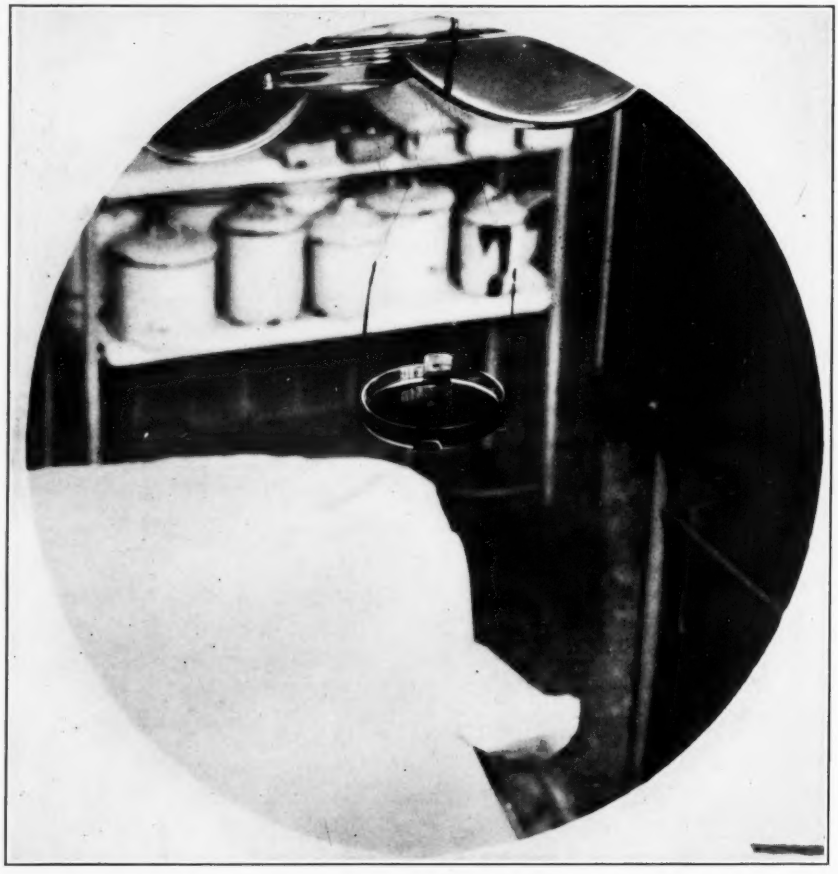

Fig. 1.—A simple Petri dish hanger suspended from operating light in field of operation.

Fig. 2 shows the result of one of the exposures after forty-eight hours of incubation. The other exposures were practically the same (Fig. 3). Aside from the identification of the presence of staphylococci and the hemolytic streptococcus, no effort was made to carry out

Fig. 2.—Hanging Petri dish culture exposed during surgical clinic; forty-eight-hour incubation.

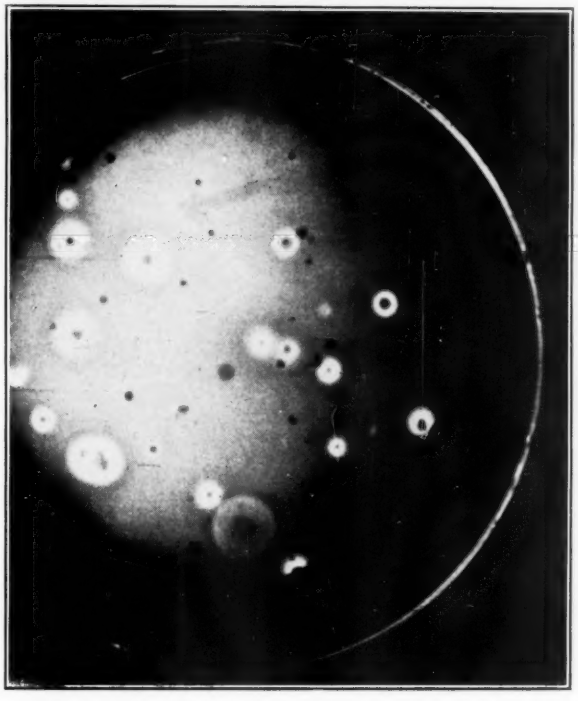

Fig. 3.—Another hanging Petri dish culture; forty-eight-hour incubation.

analytical percentage studies, as this work has been done repeatedly by others.

Ives and Hirshfeld,[3] in a study of twenty-two similar exposure cultures, found:

Average percentage *Staphylococcus aureus*	6.9	88.4
Average percentage *Staphylococcus albus*	81.5	
Average percentage remainder, yeasts, molds, etc.	11.6	
	100	

A little dust was wiped from a wall with a gauze wet with sterile water and a little of the squeezed-out fluid sprayed into a blood agar Petri dish and incubated for forty-eight hours (Fig. 4).

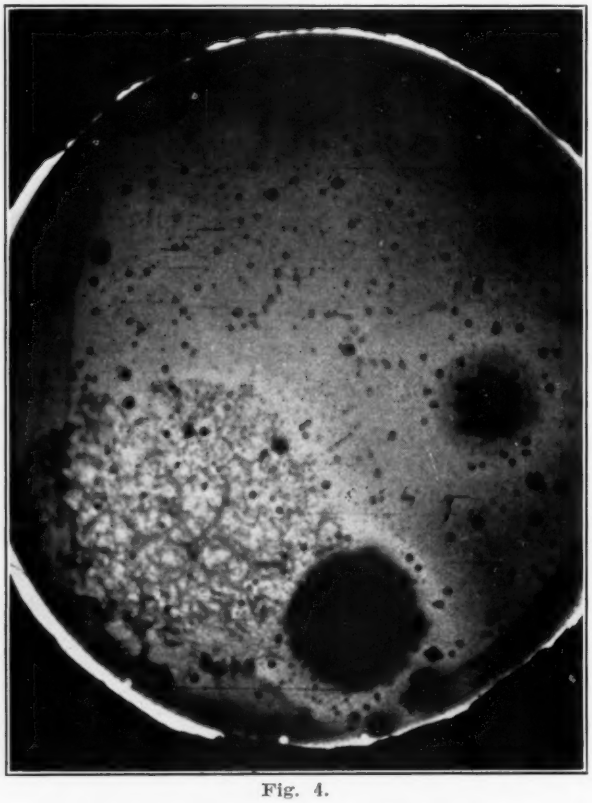

Fig. 4.

Fig. 5.

Fig. 4.—Culture of a little dust on operating room tiled wall.

Fig. 5.—Wounds thus treated uniformly heal kindly without any induration or irritation.

2. Gentle scrubbing of a surgical wound with soap and water before closure does not militate in the slightest degree against ideal healing.

This series of twenty-four routine laparotomy and other wounds indicated that gentle scrubbing with soap and water before closure did not interfere in any way with proper wound repair (Fig. 5). On the contrary, we believe from our experience that wounds thus treated heal uniformly most kindly in that there is a very noticeable lack of that

type of wound healing characterized by what might appropriately be termed the questionable stage during which, because of suspicious induration and signs of irritation, with slight elevation of temperature the surgeon has some anxiety as to just what will develop by the next dressing inspection. We are convinced that the debacterialization of the wound also removes wound detritus and blood which, if left, form sufficient nutrient material for the infecting organisms to give this expression of their presence before succumbing to the gathering forces of natural resistance of the individual patient. An appropriate term to describe the type of primary healing obtained by this method would be complete placidity.

The actual cleansing procedure and satisfactory end results were found in such major operative procedures as the following:* radical breast amputation for carcinoma, amputation of thigh for senile gangrene, cholecystectomy, open reduction of fracture of thigh, and Wangensteen's operation for a huge ventral hernia with utilization of a four-inch strip of fascia lata necessitating a twenty-inch thigh incision; both wounds healed perfectly.

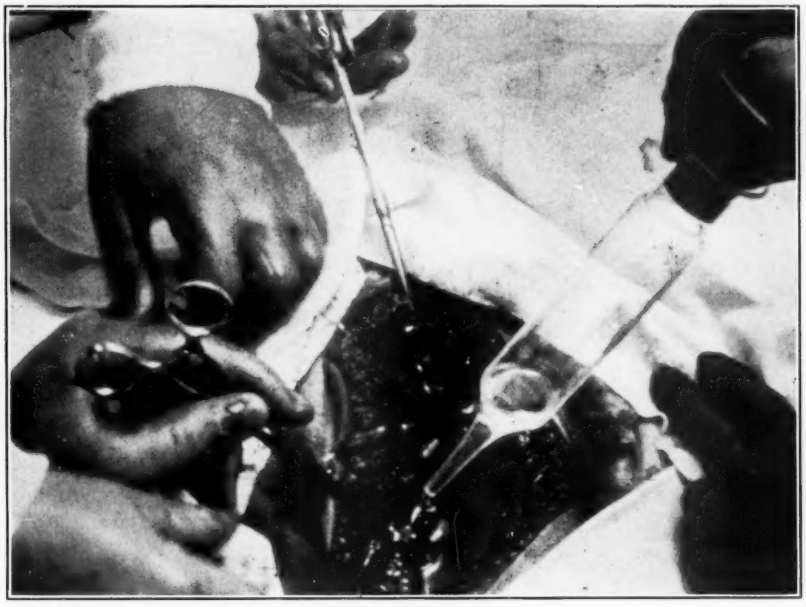

Fig. 6.—After peritoneum is closed, sterile water is swished with a syringe into wound and 0.5 c.c. transferred to sterile nasal spray and cultured.

3. In a surgical wound proved to be contaminated, how much will soap cleansing debacterialize it?

In performing a splenectomy for a large primary hemangioendothelioma of the spleen, after closure of the peritoneum, 10 c.c. of sterile water is swished back and forth in the wound with a glass syringe (Fig. 6); then 5 c.c. of the wound fluid is withdrawn, placed

*Colored films depicting the actual cleansing procedure and satisfactory end results in such major operative procedures as those listed were shown in the presentation.

in a sterile one-ounce nasal spray and 0.5 c.c. sprayed into a blood agar Petri dish. (After forty-eight hours' incubation, the culture appeared as shown in Fig. 7.)

The wound is then methodically cleansed, beginning at one end and completely cleansing the bottom and sides to the other end, with soap solution and sterile water. Ten cubic centimeters of sterile water is again swished in the wound, 0.5 c.c. of wound fluid sprayed into a blood agar Petri dish. (After forty-eight hours' incubation, the culture appeared as shown in Fig. 8.)

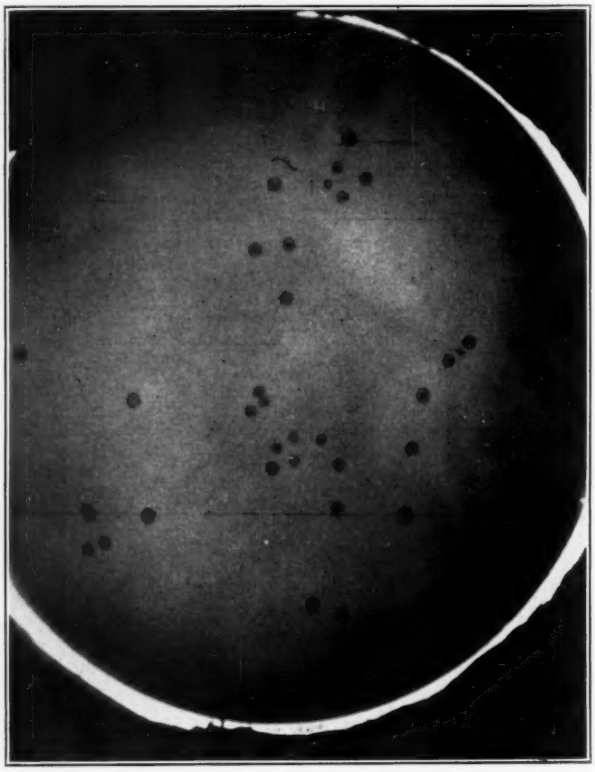

Fig. 7.—Culture from splenectomy wound before wound was cleansed with soap and water.

The wound is now packed with dry gauze and the wound lips closed over it with towel clips. The skin area around the wound is cleansed with soap and water, followed by alcohol sponging and painted with the surgeon's preferred dye. All drapes and instruments are removed.

The surgeon and assistants either put on fresh gloves or wash the ones they have on thoroughly with liquid soap and sterile running water. Fresh drapes are applied. A tray of freshly sterilized instruments and fresh suture material for closing the wound is properly placed. On no account should any instrument which has laid exposed on the reserve instrument table be used, as unquestionably particles of bacteria-laden dust have fallen on them and may be easily transmitted into the wound.

All bleeding points, no matter how small, are controlled by lightly touching with the point of the coagulating current, by pressure, or by ligation with the finest catgut. Perfect hemostasis is imperative.

Wound culture before cleansing	66 colonies
Wound culture after cleansing	4 colonies
A debacterialization of	93.8%

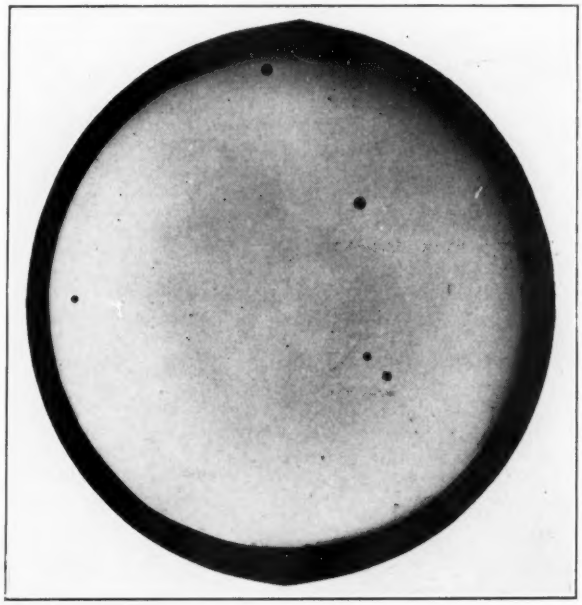

Fig. 8.—Culture from splenectomy wound after cleansing with soap and water.

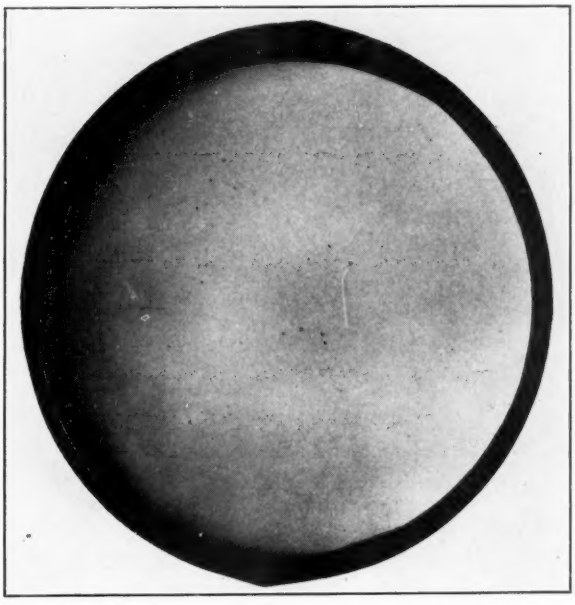

Fig. 9.—With increasing attention to minute details through routine practice, the percentage of negative plate cultures made after the wound cleansing will steadily rise.

This, in our experience, may be considered a fair average. Naturally, the result will vary directly with the thoroughness with which the procedure is carried out.

In laparotomies where a hollow viscus has been opened and in cases of acute appendicitis, etc., cleansing should be done with especial thoroughness to diminish the chances of a colon bacillus wound infection. The more adept and thorough one becomes after using the method routinely, the larger the number of 100 per cent efficiency demonstrations.

Any possible infection of the wound in spite of it will depend largely on the quality of application by the individual surgeon of those surgical mandates which are imperative to obtain good wound repair, such as avoidance of (1) tension, (2) interference with blood supply, (3) unnecessary trauma, (4) excessive use of catgut, (5) mass ligation, and (6) imperfect hemostasis. The maximum amount of physiologic rest for the wound must be provided.

Ives and Hirshfeld[3] state: "All wounds are heavily contaminated with bacteria presumably from the skin of the patient and the air of the operating room. Many of these organisms are known to be nonpathogenic, but the staphylococci form a not inconsiderable portion of the total. In spite of the presence of these bacteria, only about 5 per cent of the wounds become infected, so that factors other than the mere presence of bacteria, such as the resistance of the patient and the condition of the wound itself, must play an important role in the development of infection." "However," they add, "if the staphylococci as a group are responsible for the majority of wound infections, one may rightly assume that the contamination of wounds with these organisms is the cause of many postoperative wound infections. Our inability to reduce the incidence of infection below 5 per cent may well be due to neglect of this source of contamination."

Doubtless we have all had, time and again, a series of 100 or more cases in which there was not a single instance of wound infection, and we took pride in the fact that apparently there was no weak link in our aseptic routine. Yet, who among us has not had the nerve-racking, harrowing experience of a run of unexplainable, unwarranted, clinical wound infections? What a relief when the average incidence subsides to 4 or 5 per cent.

The experience of Hart and his colleagues is one which warrants constant repetition in the telling:[2]

"In 1925, confronted by a series of unexplained infections, a well known bacteriologist was asked to survey critically the entire operating room technic. He reported that there was no break in it to account for the infections. In this study, he completely ignored the air, including the dust in the air.

"After the opening of the Duke Hospital in 1930, at which time we were particularly anxious to avoid any unfavorable results in a new institution, we were confronted with a mounting percentage of infections in clean operative wounds. A most careful study of our aseptic technic, extending over two years, failed to show any flaw in the sterility of instruments, linen, ligatures, or other material used in the course of the operations.

"The greatest source of contamination was then most strikingly shown to be from the air. An attempt was made to free the operating rooms of these organisms (principally staphylococci) by exclusion and sterilization. Double doors were installed to prevent air currents from the wards. The carbolic spray was found ineffectual; the walls and ceilings were repainted, et cetera.

"The room so treated was found to be practically free from organisms. When occupied for the first operation, there was a rapid contamination of the air with staphylococci. We then showed that this contamination of the air with staphylococci at any place in the hospital or medical school was directly dependent on the number of occupants and the duration of occupancy."

Meleny[5] recently has called attention to "the importance and present neglect of anaerobic bacteriology in the operating room." The cleansing of the wound as here described should conceivably diminish the chance that any such should remain to develop after wound closure.

The question may be raised: "Is it not possible that the remnant of soap left in the wound may act as a powerful germicide?" The soap that we have used through our experiments differs from the U.S.P. green soap in that in place of linseed oil the soya bean oil and corn oil are used with pure potassia. Cultures made with weak solutions of this soap show that bacteria thrive in it.

Inasmuch as it requires some experience to judge the proper strength of soap solution to be satisfactory as a cleansing agent and yet not be strong enough to blacken the tissues when used, we append here the directions followed by the operating room nurses in preparing it.

One pound of "operative" green soap* is thoroughly dissolved by boiling it in 4,000 c.c. of water, put in flasks, and autoclaved. Equal parts of this and sterile water are mixed together before using it at the operation; of this latter mixture, one or more ounces (depending on size of wound) is put in a suitable open top container and placed on the overhanging instrument rack available to the surgeon. Beside it are placed a vessel of sterile water and a pile of gauze sponges.

A gauze sponge is dipped first into the water and then lightly into the soap solution and applied to the wound. If the tissues tend to turn black, use less soap with the following swab. About a 6 per cent

*"Operative" green soap obtained from Theodore B. Robertson Products Company, Inc., 700-704 Division St., Chicago, Ill.

soap water solution contacts the tissues. We feel that a minimum cleansing time limit should be recognized and routinely make this two minutes by the clock for small wounds and may use up to five or more minutes in larger ones.

SUMMARY

The prime objective of this presentation was to demonstrate through personal experience that the cleansing with soap and water before closure of clinical wounds does not interfere in any way with ideal wound healing. We found this to be true in our series of over 200 consecutive wounds thus treated; there was no single instance of interference with primary wound healing due to it.

Another objective was to ascertain the relative value of the method in actually debacterializing a clinical wound. This we have found to be a variable quantity directly proportional to the thoroughness with which the procedure is carried out. A fair average would be 90 per cent efficiency. It must be remembered that the few seconds' exposure of the culture material to the air contamination, while transferring the wound washings after the cleansing, might permit of and be the direct cause of a few colonies developing after incubation.

As regards the incidence of secondary or hematogenous-borne wound infection, there were two instances in our series. One patient, ten days after a supravaginal hysterectomy, was found to have, in the lower end of the incision, a small broken-down, infected blood clot. This, we believe, was due largely to imperfect hemostasis before closing the wound. The other instance was that of a stitch abscess developed around a tension suture which the resident had overlooked and failed to remove until the fifteenth postoperative day.

While the problem of secondary clinical wound infections involves many imponderable factors, such as the general constitutional status of the patient and the presence or absence of a natural or inherited resistance to infection, we believe from the low incidence of secondary infection in our series that the mechanical cleansing in directly removing blood clots, broken-down fat cells, and wound detritus also greatly diminish the chance of a *locus minoris resistentiae* developing to form a nidus in which floating organisms may find lodgment with available nutrition and multiply. Every surgical wound develops a sticky, fibrinous nutrient film which catches and holds bacteria and dust as would flypaper. This mechanical cleansing removes it with all other wound detritus and thus not only diminishes the chances of infection but actually aids in ideal wound repair.

CONCLUSIONS

1. The air of every operating room is practically always badly contaminated with staphylococci and streptococci. The incidence of pri-

mary wound infection with these organisms averages 4 to 6 per cent, but at times may be as high as 20 per cent.

2. Every surgical wound develops a sticky fibrinous nutrient film which catches and holds bacteria and dust as would flypaper.

3. The amount of contamination and potential source of wound infection is directly proportional to the size of the wound and the length of time the air exposure continues.

4. Mechanical cleansing with soap and water just before closure of wound very efficiently and harmlessly removes this chance of primary wound infection with staphylococci, streptococci, etc.

5. The method actually aids in ideal wound repair as evidenced by the very high per cent of wounds healing with "complete placidity," no redness, induration, or irritation such as often seen and noted in wounds which just manage to pass muster as healing per primam.

We wish to acknowledge our indebtedness to Dr. W. D. Stovall, Director of the Wisconsin State Laboratory of Hygiene, for his sympathetic, cooperative suggestions and directions in the bacteriologic field.

April 1, 1939: We have continued throughout the winter and spring months to use this method. It is now routine in all operating rooms. Air cultures at times, due to upper respiratory infections in surgeons, nurses, and other operating room attendants, have shown terrific contamination, but primary wound infections have been practically nil; whereas, in the past during these seasons we have labored under a dreaded expectation of an appreciable rise in primary wound infections. Wound cultures after cleansing now show a very high percentage of negative results (Fig. 9). We are convinced that it is a harmless, inexpensive, efficient procedure and urge every surgeon, with the cooperation of a bacteriologist, to carry out the same convincing experiments.

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LESIONS OF THE INTERVERTEBRAL DISK AND LIGAMENTUM FLAVUM OF THE LUMBAR VERTEBRAE

An Anatomic Study of 75 Human Cadavers

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I. DEGENERATIVE LESIONS OF THE INTERVERTEBRAL DISK

IN A NORMAL adult intervertebral disk, the cartilage plate which overlies the cortical bone of the vertebral body, is intimately blended on its intervertebral surface with a layer of fibrocartilage which gives attachment to the fibers of the annulus fibrosus. The annulus serves as an envelope for the gelatinous, relatively incompressible nucleus pulposus. Most investigators believe that the disk is avascular, although Böhmig,[1] examining 70 vertebral columns from the embryonal state to the age of 30 years, found blood vessels in the intervertebral disks up to the age of 25 years; while Smith[2] demonstrated nutritive channels within the intervertebral disk which communicated directly with blood channels from the spongiosa of the vertebral body. Jung and Brunschwig[3] found nerve fibers only in the anterior and lateral longitudinal ligaments; never within the disks.

A cross section of the disk in an infant reveals a gradual change from the hyaline type of cell at the periphery to an almost complete disappearance of cellular structure within its interior. There is a gradual loss of chondromucoid substance with isolated cartilage cells in its lacunae, and in the central portion of the disk are small clumps of cells which resemble prechondral tissue, the remaining notochordal cells. Microscopically, the adult disk shows a very loose network of fibrous tissue, in the meshes of which lie a profusion of connective tissue and cartilage cells.

The commonest lesion of the spine, according to Schmorl,[4] is prolapse of the nucleus pulposus into the spongiosa of the vertebral body (Schmorlsche Knötchen), which he found, single and multiple, in 38 per cent of several thousand spines removed at necropsy. The nuclear material is extruded through a defect in the cartilage plate, which may be developmental, traumatic, or infectious in origin, into the spongy bone of the vertebral body by external forces transmitted to the disk and by the turgor of the nucleus pulposus. Petter[5] found that an average pressure of 30.2 pounds was required to reduce an average expansion

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of the intervertebral disk of 1.08 mm. The semifluid invading disk material becomes transformed into cartilage by hyperplasia of its cartilage cells and is surrounded by vascular proliferation and engorgement and then by enchondral ossification which may extend into and involve the entire intervertebral disk. As shown by Püschel[6] and by Keyes and Compere,[7] the defects in the cartilage plate of the intervertebral disk open avenues for dehydration, with loss of the semifluid nucleus; the disk becomes narrowed and may disappear and the adjacent vertebral bone undergoes sclerosis and marginal proliferation. Fibrillation of the cartilage plate is analogous to the fibrillation of the cartilage of other joints which is characteristic of degenerative (osteo-) arthritis and, similarly, may be attributed to chronic stress and strain.

Identical changes have been reproduced in animals by Keyes and Compere, who noted (1) that, if the cartilage plate of the intervertebral disk of a dog was injured by a scalpel or drill, nuclear material prolapsed into the spongiosa of the adjacent vertebrae with the formation of typical cartilage nodes; and (2), if the nuclear material was allowed to escape, the rest of the disk became thinned out and the margins of the adjacent vertebrae hypertrophied and sclerosed. I have observed similar degenerative changes in three adult rabbits in which the lumbosacral disks were incised anteriorly and the nuclear content permitted to escape. This experience is supported clinically by Pease[8] and Milward and Grout,[9] who demonstrated narrowing of the intervertebral disk and localized osteoarthritis of the adjacent vertebrae following injury to the disks posteriorly during lumbar puncture.

Although Schmorl believed that protrusions of the intervertebral disk into the vertebral body were of no clinical significance, Schanz[10] suggested the possible relationship between these prolapses and backache, and this belief has been supported by Mau,[11] Müller,[12] Dittrich,[13] Calvé and Galland,[14] Geist,[15] Sashin,[16] Joplin,[17] Ayers,[18] Keyes and Compere,[7] and others. The relationship of narrowing of the intervertebral disk with secondary subluxations of and arthritic changes in the apophyseal (intervertebral) joints to backache and the sciatic syndrome has been stressed by Ayers,[18] Williams,[19] Hadley,[20] and Oppenheimer.[21]

The lumbar spines of 75 adult male human cadavers, aged 45 to 80 years, were sectioned in the midsagittal plane and the relation of the intervertebral disks, vertebral bodies, intervertebral foramina, neural arch, and ligamentum flavum to each other and to the contents of the spinal canal were studied. Narrowing of the intervertebral disk with fibrillation of the fibrocartilage and dehydration of the nucleus pulposus was noted between the fifth lumbar and first sacral vertebrae in 50 specimens; between the fourth and fifth lumbar vertebrae in 36 specimens; between the third and fourth lumbar vertebrae in 27; and between the second and third lumbar vertebrae in 19 specimens. These disk changes were associated in all specimens with varying amounts of

lipping and spur formation of the adjacent margins of the vertebrae (Figs. 1 and 2). In 2 specimens the disks between the third, fourth, and fifth lumbar and first sacral vertebrae were expanded and associated with porosity of the vertebral spongiosa (Fig. 1*d*). Schmorl attributed such disk changes to the turgor of the nucleus pulposus; Moffat[22] believed these expansions of the disk to be due to hypertrophy and proliferation of its cellular elements. Protrusions of the intervertebral disk into the vertebral body (Schmorl's nodes) were found extending into the third lumbar vertebra in 6 specimens, into the fourth lumbar vertebra in 4 specimens, into the fifth lumbar vertebra in 2 specimens, and into the first sacral vertebra in 1 specimen. This occurrence was multiple in the same specimen in 3 instances and single in 4 specimens (Figs. 2 and 3).

Forward displacement of a vertebra on the vertebra below, associated with bilateral pedicle defects (anterior spondylolisthesis), was present in 5 specimens: between the fifth lumbar and first sacral vertebrae in 2, between the fourth and fifth lumbar vertebrae in 2, and between the third and fourth lumbar vertebrae in 1 (Fig. 4). The intervertebral disk at the site of the anterior spondylolisthesis was narrowed or almost absent and there was considerable bony proliferation of the superoanterior margin of the body of the lower vertebra, acting as a shelf to support the slipping vertebra above. The posterosuperior margin of the lower vertebra produced a prominent intraspinal protrusion, yet in no instance was there abnormal tension on the caudal nerve roots. The neural canal is large in this region and permits considerable shift of the roots of the cauda equina.

Posterior displacement of the fifth lumbar vertebra on the sacrum has been described by Ferguson[23] and his associates as a cause of low back pain, the lesion having been demonstrated in 235 (20.3 per cent) of 1,157 patients with low back and sciatic pain (Kimberley[25]). This displacement measures from $\frac{2}{16}$ to $\frac{7}{16}$ inch (Smith[24]). These authors differentiate the developmental type, associated with an unstable fifth lumbar vertebra, from the acquired type, due to true atrophy of the intervertebral disk. In my series the posterior margins of the fifth lumbar vertebra extended posterior to that of the sacrum for a distance of $\frac{2}{16}$ to $\frac{4}{16}$ inch in 9 specimens and was associated with degenerative changes and narrowing of the lumbosacral intervertebral disk and with marginal proliferation (Fig. 5). There was a settling of the fifth lumbar vertebra downward and backward, and this posterior displacement was made more apparent by bony proliferation at the posteroinferior margin of the fifth lumbar vertebra. In no instance was there an associated defect in the neural arch, vertebral body, or its accessory processes, and in only one instance were the planes of the lumbosacral facets less than 45 degrees from the sagittal plane of the body.

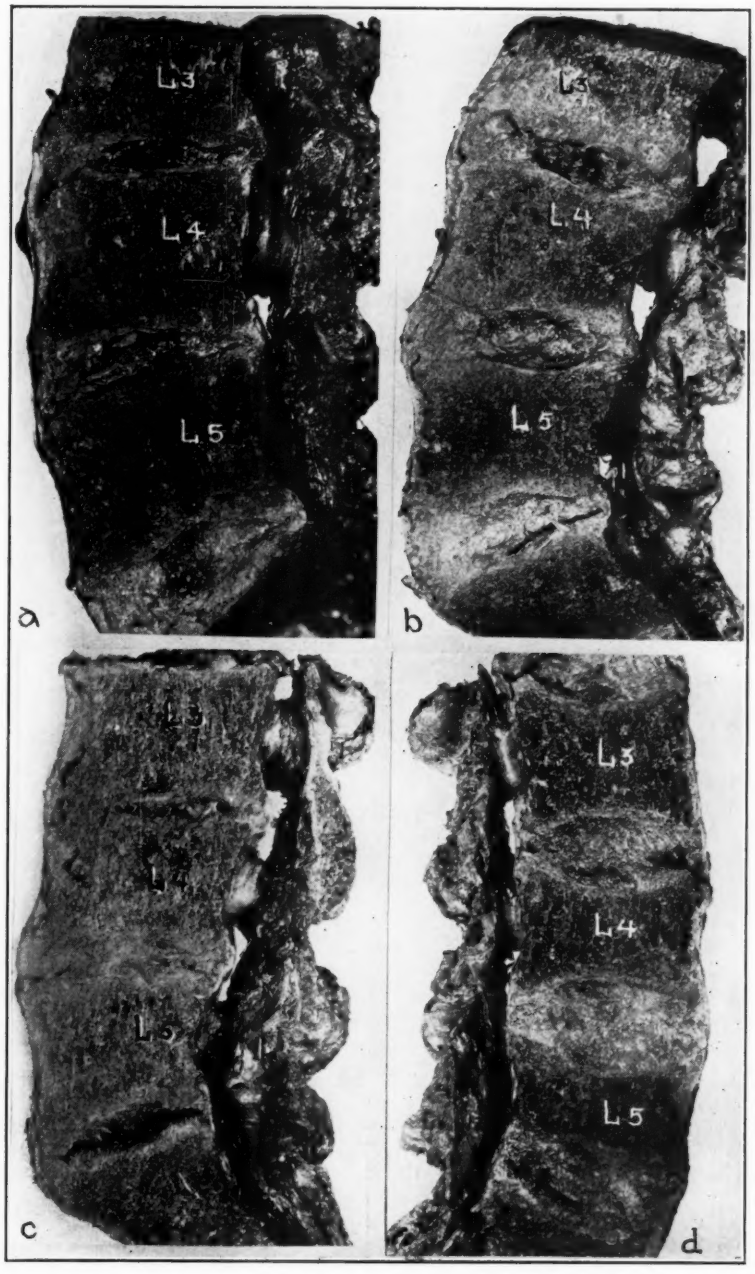

Fig. 1.—Lumbar spine, midsagittal sections. *a*, Fibrillation, dehydration, brown pigmentation, and narrowing of the intervertebral disks, associated with marginal bony proliferation and with protrusion of the disks posteriorly into the spinal canal. *b*, Similar changes to those shown in *a*, associated with sclerosis of the adjacent borders of the vertebral bodies, especially marked at the inferior border of the third lumbar vertebra. *c*, Narrowing, dehydration, and fibrillation of the intervertebral disks, with bony fusion between the third and fourth lumbar vertebral bodies due to ossification of the anterior one-third of the corresponding disk. *d*, Expansion of the intervertebral disks, especially marked between the fourth and fifth lumbar vertebrae, and associated osteoporosis and compression of the vertebral bodies.

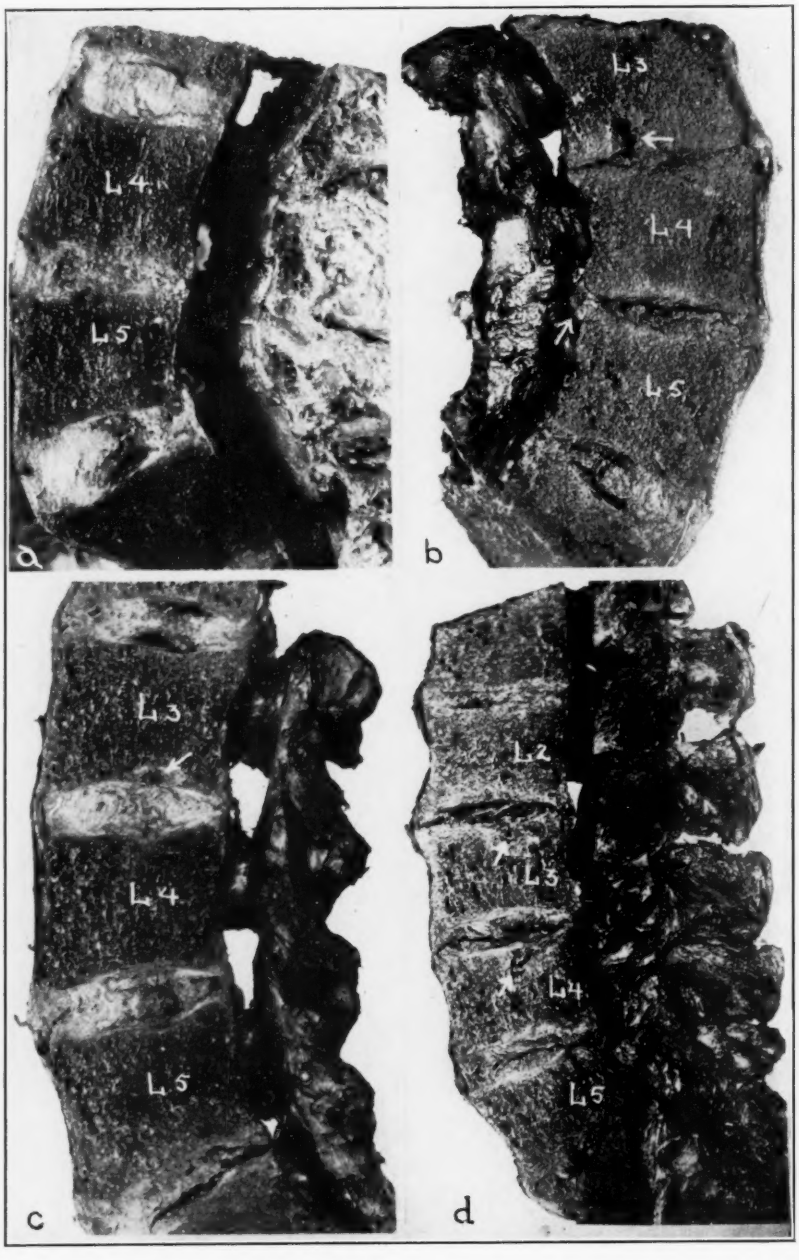

Fig. 2.—Lumbar spine, midsagittal sections. *a*, Narrowing, dehydration, and brown pigmentation of the intervertebral disk between the fourth and fifth lumbar vertebrae, with sclerosis of the adjacent vertebral margins. *b*, Protrusion of the intervertebral disk into the inferior portion of the third lumbar vertebra and protrusion of the disk between the fourth and fifth lumbar vertebrae posteriorly into the spinal canal. *c*, Protrusion of the intervertebral disk into the inferior portion of the body of the third lumbar vertebra with surrounding bony sclerosis. *d*, Protrusions of the disk into the superior portion of the bodies of the third and fourth lumbar vertebrae.

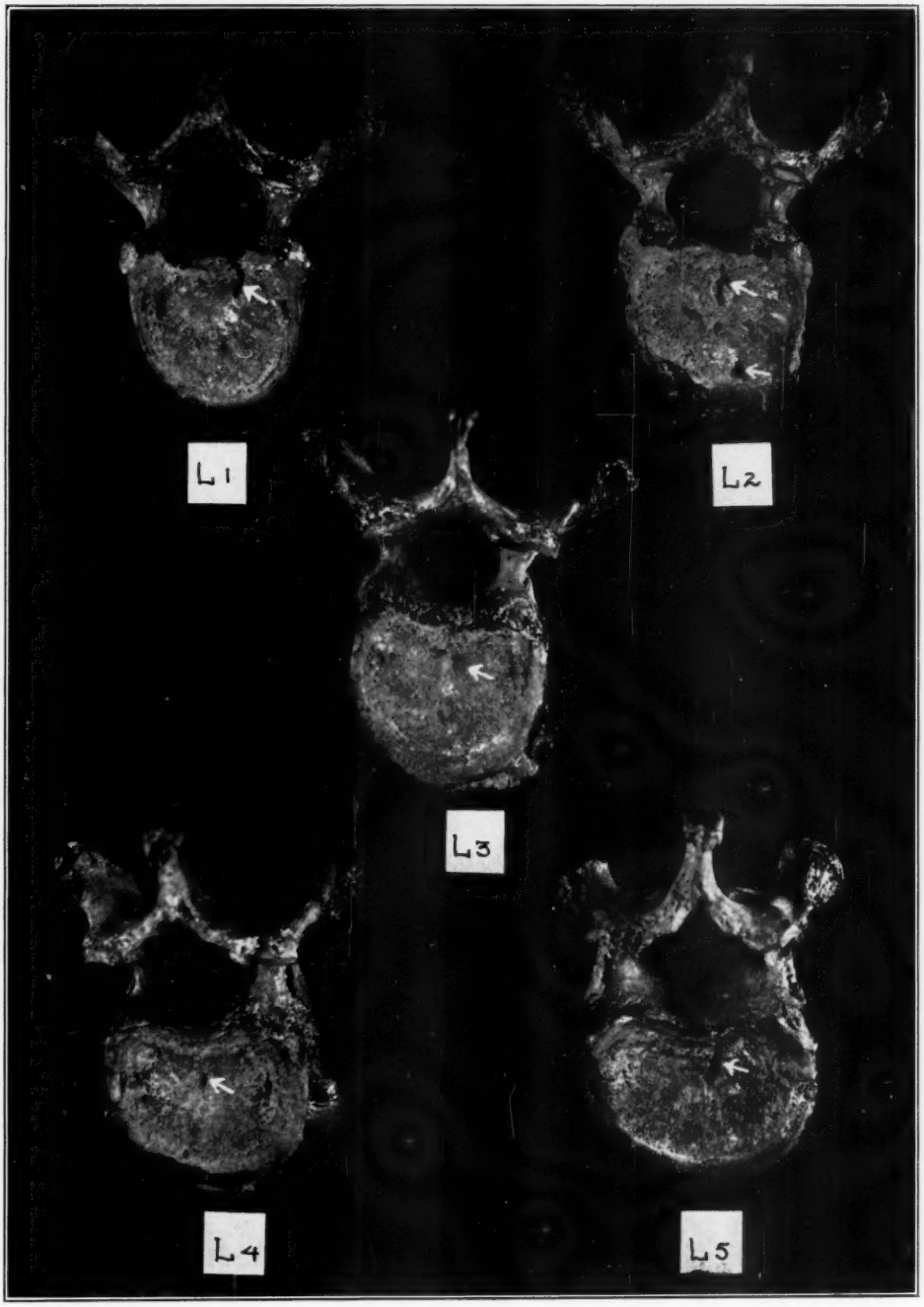

Fig. 3.—Defects in the inferior surfaces of macerated lumbar vertebrae from the same specimen due to intervertebral disk protrusions into the spongiosa. The rim of bone, present anteriorly and laterally but not posteriorly, is the epiphyseal ring which has fused with the vertebral body.

The histories of 25 cases in this series of 75 specimens were reviewed. Although there were narrowed disks in 24 cases, protrusions of the disk into the vertebral bodies in 4, and posteriorly into the spinal canal in 9, backache was an infrequent and minor complaint in this series, and in no instance had the patient experienced the sciatic pain syndrome.

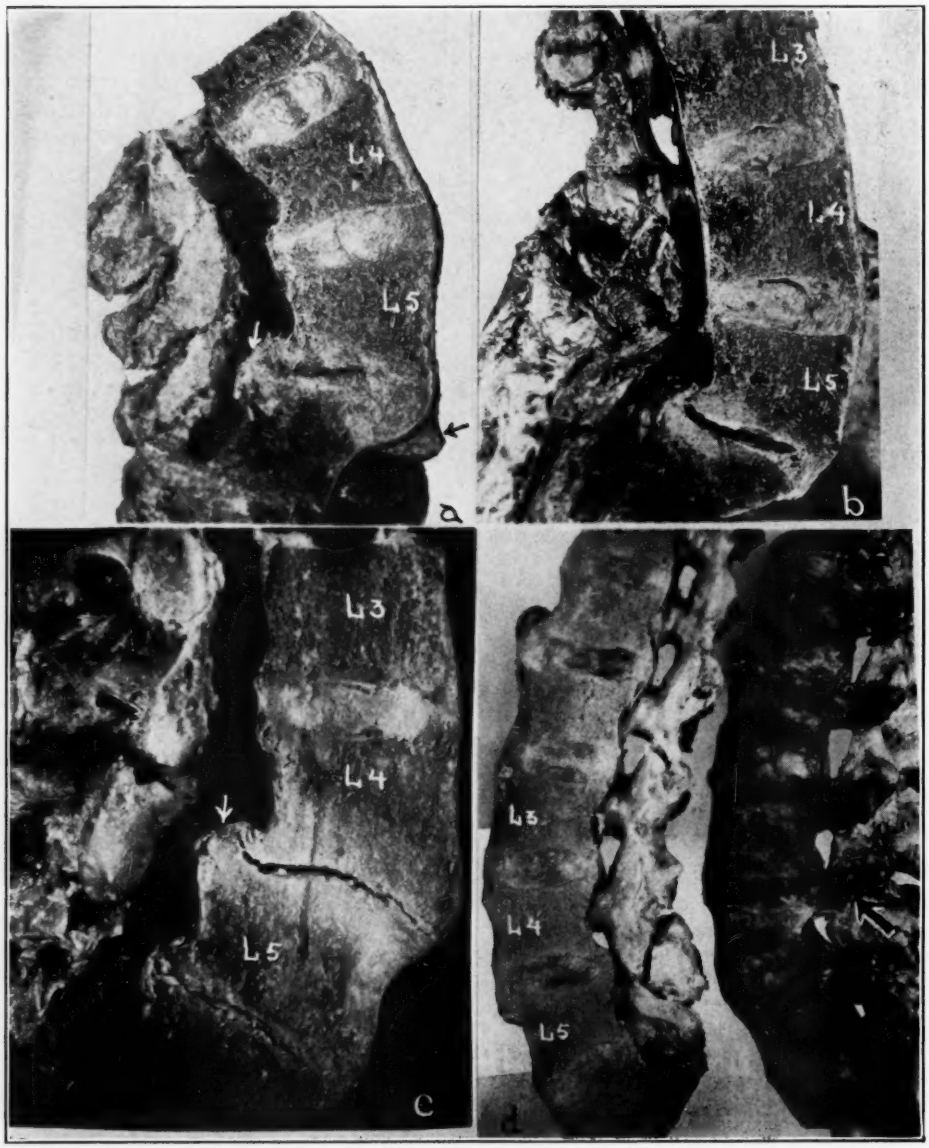

Fig. 4.—Lumbar spine, midsagittal sections. *a*, Anterior spondylolisthesis of the fifth lumbar vertebra with marked narrowing of the lumbosacral disk, bony proliferation of the anterosuperior margin of the first sacral vertebra, and encroachment on the spinal canal by the hypertrophied posterosuperior margin of the first sacral vertebra. *b*, Anterior spondylolisthesis of the fifth lumbar vertebra. *c*, Anterior spondylolisthesis of the fourth lumbar vertebra. The corresponding disk has disappeared and the adjacent vertebral bodies are in direct contact and markedly sclerosed. Encroachment on the caliber of the spinal canal by the hypertrophied posterosuperior border of the fifth lumbar vertebra is apparent. *d*, Anterior spondylolisthesis of the fourth lumbar vertebra. The site of the pedicle defect is marked by an arrow.

II. POSTERIOR PROTUSIONS OF THE INTERVERTEBRAL DISK

Kocher[26] in 1896 reported a case of ruptured intervertebral disk without cord compression in a man who had died of injuries following a fall from a height of 100 feet. In 1911 Middleton and Teacher[27] and Goldthwait[28] reported cases of cord compression due to changes in the intervertebral disks. Extradural tumors arising from the intervertebral disk have been described variously as "intervertebral disk chondroma"

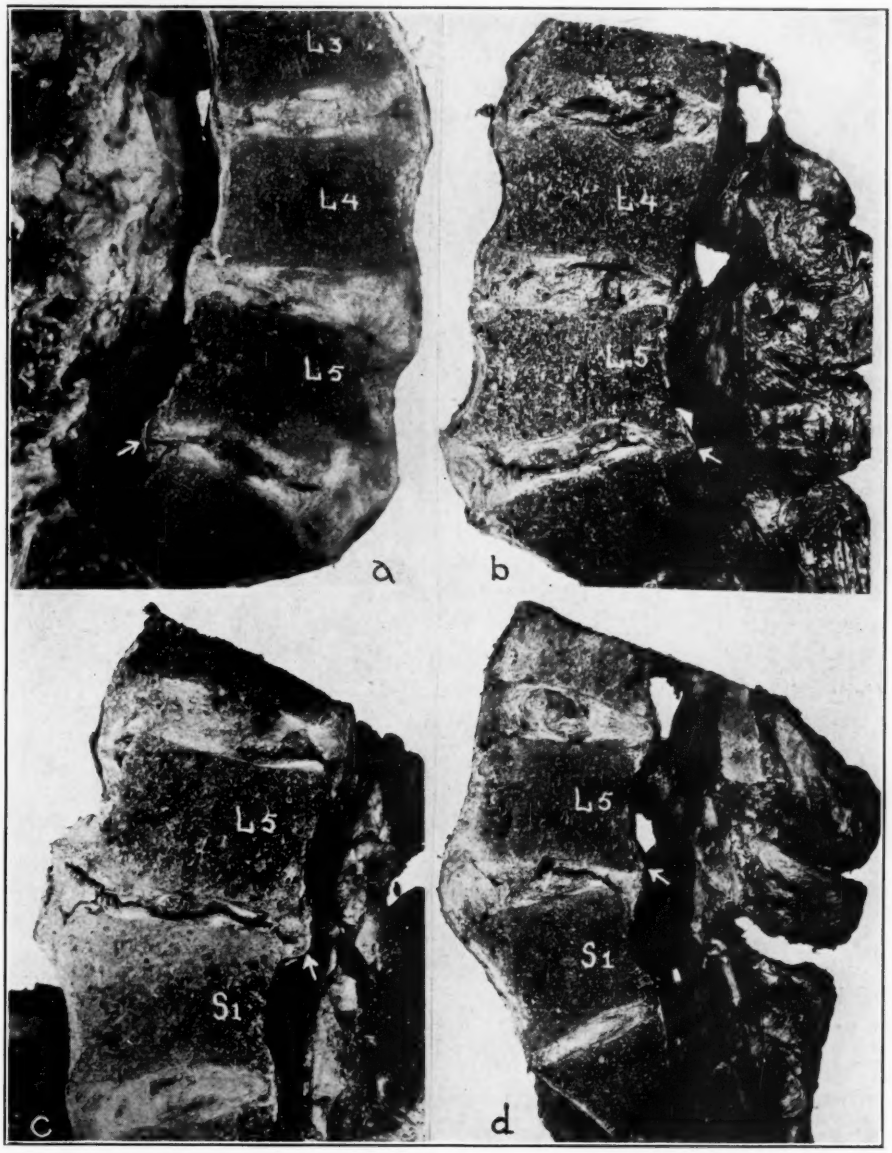

Fig. 5.—Midsagittal sections. The posterior border of the fifth lumbar vertebra in all the specimens lies posterior to the corresponding border of the first sacral segment, the posteroinferior border of the fifth lumbar vertebra constituting a definite protrusion into the spinal canal. There are degenerative changes in the intervertebral disks, especially at the site of "posterior displacement"; i.e., the lumbosacral disks.

by Bailey and Bucy,[29] "ventral extradural chondroma" by Stookey[30] and Adson,[31] "myxochondroma" by Veraguth,[32] "fibroma" by Alajouanine and Petit-Dutaillis,[33] "fibro-chondroma" by Crouzon, Petit-Dutaillis, and Christophe[34] and by Ott and Adson,[35] "Schmorl's nodule" by Klinge,[36] Kortzeborn,[37] and von Péchy,[38] "loose cartilage from the intervertebral disk" by Dandy[39] and "ecchondrosis" by Elsberg.[40]

The conception of these lesions as posterior herniations of the nucleus pulposus was initiated by the researches of Andrae[41] and Schmorl.[42] Andrae found 56 cases of posterior nodules of the intervertebral disk in 368 spines (15.2 per cent), appearing as small, pea-sized projections on the anterior surface of the spinal canal, 20 in males and 36 in females. There were none in patients below 30 years of age and the majority were in patients above 50 years of age. In 25 cases there were more than one nodule and as many as 7 nodules occurred in a single specimen. Andrae demonstrated direct communications between the nucleus pulposus and posterior disk protrusion in 16 specimens. Neither he nor Schmorl attributed clinical significance to these lesions.

Due largely to improvement in diagnostic measures, especially in the use of iodized oil intraspinally,[43-46] large series of these lesions causing cord or nerve root compression have been reported by Love and Walsh[47] (113 posterior disk protrusions in 100 patients),* Barr[48] (83 cases), Glorieux[49] (25 cases), Fincher and Walker[50] (24 cases), Haggart[51] (25 cases), Poppen[52] (26 cases), and small series by Peet and Echols,[53] Slaughter,[54] Sherwood and Berens,[55] Paltrinieri,[56] Simonds,[57] Flothow,[58] Furlow,[59] Steele,[60] and others. Botts[61] found posterior protrusions of the intervertebral disk into the spinal canal in 16 per cent of 50 human cadavers.

In my series of 75 adult lumbar spines, unilateral posterior herniations of the nucleus pulposus were demonstrated in 4 instances: one between the second and third lumbar vertebrae (¼ inch in diameter), one between the third and fourth lumbar vertebrae (½ inch in diameter), one between the fourth and fifth lumbar vertebrae (¼ inch in diameter), and one arising from the lumbosacral disk (3/16 inch in diameter). Posterior bulging of the annulus fibrosus of the disk across its entire width, without true herniation, and formed in great part by the hypertrophied posterior margins of the adjacent vertebrae, was found in 21 instances between the fifth lumbar and first sacral vertebrae, 19 instances between the fourth and fifth lumbar vertebrae, 9 instances between the third and fourth lumbar vertebrae, and once between the second and third lumbar segments. In each instance there were associated degenerative changes throughout the intervertebral disk (Fig. 6).

Camp and Barr in their large series of cases found the association of narrowing of the intervertebral disk with marginal bony proliferation

*In a more recent report by these authors, this series includes 200 cases (Walsh, M. N., and Love, J. G.: The Syndrome of the Protruded Intervertebral Disk, Proc. Staff Meet., Mayo Clin. 14: 230, 1939.

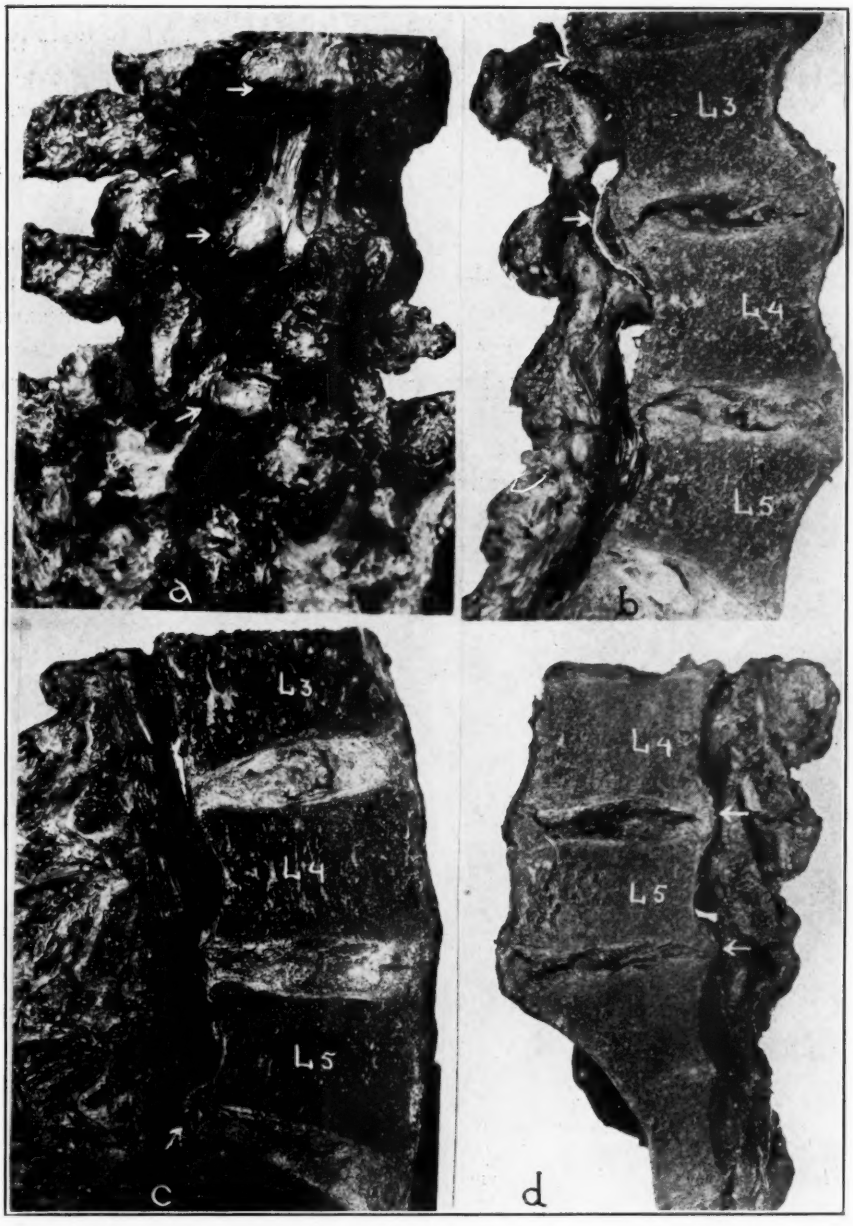

Fig. 6.—*a*, Posterior view of the vertebral bodies and intervertebral disks; *b*, lateral midsagittal view of the same specimen. There are posterior protrusions of the intervertebral disks between the second, third, fourth, and fifth lumbar vertebrae, associated with degenerative changes throughout the entire disks. A large intraspinal protrusion, measuring ½ inch in diameter and extending 3/16 inch posteriorly, involves the intervertebral disk between the third and fourth lumbar vertebrae to the left of the posterior longitudinal ligament. *c*, Midsagittal section; posterior protrusion of the lumbosacral intervertebral disk with encroachment of the spinal canal. *d*, Midsagittal section; posterior protrusion of the intervertebral disks between the fourth and fifth lumbar and the fifth lumbar and first sacral vertebrae. The intervertebral disks show advanced degenerative changes.

(roentgenographic) and the site of the posterior disk protrusion frequent but not constant enough to be of significance to them. The association of these two lesions may be more definite than is apparent in their investigations, when one realizes that roentgenographic evidence of intervertebral disk changes becomes manifest relatively late in the degenerative process and only after narrowing of the intervertebral space, calcification of the disk, or marginal bony proliferation have occurred (Horwitz and Smith[62]).

In no instance, in my series, was a spinal nerve unduly compressed either within the spinal canal or at its exit through the intervertebral foramen, although the caliber of the latter frequently was diminished by the bulging disk. It is true that the relation of nerve to adjacent structures might become altered in the cadaver, but the histories of nine cases with evidence of posterior protrusion of the intervertebral disk were reviewed and in no instance had the patient experienced marked backache or the sciatic pain syndrome.

Fig. 7.—Midsagittal sections; anterior protrusion of the lateral portion of the ligamentum flavum (left), between the fifth lumbar and first sacral vertebrae, encroaching upon and narrowing the intervertebral foramina. These protrusions were found to be due to hypertrophic changes in the underlying articular facets of the apophyseal joint and not to actual hypertrophy of the ligamentum flavum.

Microscopic studies of 100 specimens of posterior disk protrusions by Deucher and Love[63] revealed annulus fibrosus and parts of the nucleus pulposus in all and the presence of notochordal cells in many. Grossly, two types have been noted, those that "pop out" when the dura is incised anteriorly and those that are firmly adherent and are removed with great difficulty. From an analysis of their pathologic studies, it becomes evident that the term "posterior protrusion of the intervertebral disk" is more accurate than that of "posterior herniation of the nucleus pul-

posus," and that the older concept of these lesions as representing extradural neoplasms arising from the cartilaginous elements of the disk posteriorly should not be entirely discarded.

III. STUDIES OF THE LIGAMENTUM FLAVUM

Extradural lesions due to hypertrophy of the ligamentum flavum first were described by Elsberg[64, 65] in 1913 and 1916 and have been reported by Towne and Reichert,[66] Puusepp,[67] Abbott,[68] Hampton and Robinson,[44] Spurling, Mayfield, and Rogers,[69] Naffziger, Inman, and Saunders,[70] Brown,[71] and Meredith and Lehman.[72]

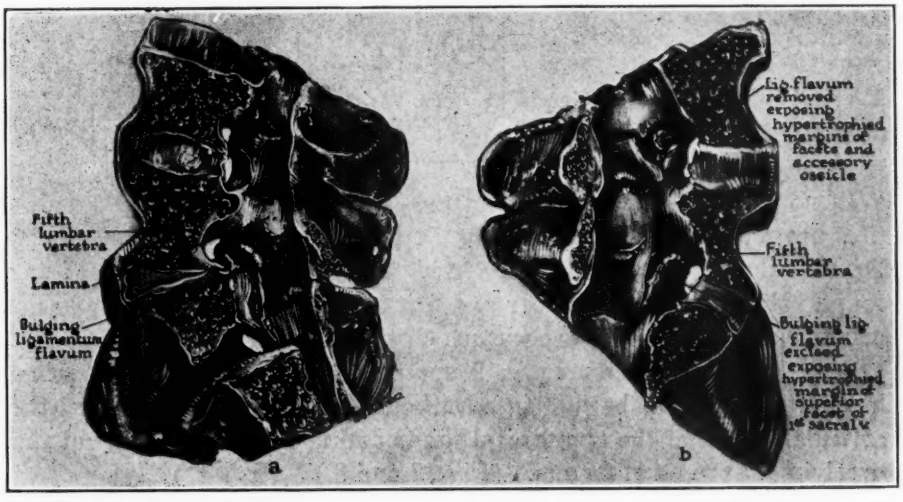
Fifth lumbar vertebra
Lamina
Bulging ligamentum flavum
a
Lig. flavum removed exposing hypertrophied margins of facets and accessory ossicle
Fifth lumbar vertebra
Bulging lig. flavum excised exposing hypertrophied margins of superior facet of 1st sacral v
b

Fig. 8.—The lesion shown in Fig. 7 is illustrated in two other specimens, before (*a*) and after (*b*) removal of the normal ligamentum flavum overlying the protrusion.

The ligamentum flavum bridges contiguous laminae, blending in the midline with the interspinous ligament, and laterally enters into the formation of the anterior capsule of the corresponding apophyseal joint. In the lumbar spine the upper portion of the intervertebral foramen is traversed by the spinal nerve, while the lower portion is a mere slit, bounded in front by the intervertebral disk and behind by the ligamentum flavum. The spinal nerve may be compressed either as it descends, medial to this slit, to leave through the intervertebral foramen below, or within the foramen itself. It has been suggested that the ligamentum flavum hypertrophies due to injury and scar tissue formation, and in almost all instances this lesion has been reported as involving the interspaces between the fourth and fifth lumbar and the fifth lumbar and first sacral vertebrae and has measured from 8 to 16 mm. in thickness. Microscopic studies have shown little except thickening of the vessel walls, fibrosis, areas of blood pigment, and calcification. Spurling and his co-workers described an associated hypertrophy of the lamina, but this has not been confirmed by other observers. The association of

hypertrophy of the ligamentum flavum with posterior protrusion of the intervertebral disk has been noted by Brown,[71] Bell and Spurling,[46] and Love.[73]

In order to determine the normal variations in thickness of the ligamentum flavum Spurling, Mayfield, and Rogers measured this structure in the region of the midlamina in 40 human cadavers, and these measurements have been repeated by me in 21 specimens.

TABLE I

		INTERSPACE				NO. OF CADAVERS
		2-3L	3-4L	4-5L	5L-1S	
Thickness of ligamentum flavum (Spurling and co-workers)	Minimum	–	2.0 mm.	2.0 mm.	2.0 mm.	40
	Maximum	–	7.0	7.0	7.0	
	Average	–	4.3	4.4	4.2	
Horwitz' series	Minimum	2.0 mm.	2.0 mm.	1.5 mm.	2.0 mm.	21
	Maximum	4.5	5.0	6.0	6.0	
	Average	3.5	3.5	3.8	3.6	

In no instance in my series did the ligamentum flavum exert undue pressure on the caudal nerve roots. Apparent forward bulging of the ligamentum flavum, which constricted the intervertebral foramen, was found between the fifth lumbar and first sacral vertebrae in 4 specimens on the right side and in 3 specimens on the left, and between the fourth and fifth lumbar vertebrae in 2 specimens on the right side. This bulge was found to be due to advanced marginal proliferation of the articular facets of the apophyseal joints and not to hypertrophy of the overlying ligamentum flavum. (Figs. 7 and 8.)

CONCLUSIONS

Recent clinical reports indicate that posterior protrusion of the intervertebral disk and hypertrophy of the ligamentum flavum are extradural lesions which are not infrequent causes of low back and sciatic pain syndromes. Since the diagnosis of these cases depends not only on abnormal neurologic and spinal fluid findings, but in great part on the use of contrast myelograms, it is important to understand that other lesions, largely the result of degenerative processes and also involving the intervertebral disk and ligamentum flavum and their adjacent structures, may be asymptomatic and yet produce defects in the intraspinal column of air or iodized oil.

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CELLOPHANE AS A WOUND DRESSING

EDWARD L. HOWES, M.D., WASHINGTON, D. C.

STERILIZED cellophane is an excellent dressing for clean wounds. It has several advantages not possessed by ordinary gauze: (1) the wound may be inspected repeatedly for evidence of infection without the necessity of changing the dressing; (2) accurate palpation of the length of the incision may be carried out at any time without contaminating the wound; (3) it does not stick to the wound crust and consequently may be removed without distressing the patient; (4) it is extremely economical; (5) it is more impervious to external bacterial contamination than gauze; and (6) the amount of seepage and hemorrhage occurring during the first twenty-four hours may be seen and used as a measure to perfect the surgical technique.

No. 600 plain cellophane with thickness of 0.0017 inch has been found to be the most satisfactory grade and is best prepared by autoclaving. The sheet is cut in a rectangle of the desired size at the operating table, and the wound and surrounding skin swabbed with ether to render it as dry as possible. The sheet is then placed directly over the incision and fastened into place by a border of adhesive plaster on all four sides. The adhesive plaster is placed half on the skin and half on the cellophane, sealing down the edges. Small droplets of blood and moisture, partially obscuring vision, accumulate on the inside of the sheet within the first few hours, but drying takes place during the next twenty-four to thirty-six hours if adequate hemostasis was obtained at the time of operation. A heat lamp is frequently applied to the abdomen to aid drying, for the comfort it gives to the patient and because the resulting vasodilatation aids healing.[1] An air vent may be left at one corner if desired, but it will not prevent the transitory steaming.

The vent should always be made after twenty-four hours if the collection is excessive, for the dry state is more conducive to healing per primam than the wet, as John Hunter pointed out long ago. A small square of gauze is then placed over this opening to prevent soiling of the bedclothes. Excessive collections of fluid were only found when hemostasis was inadequately obtained or when the wounds were going to have untoward healing. For example, they occurred within the first twenty-four hours when large amounts of catgut were placed in the subcutaneous fat and when the skin edges were improperly approximated and both technical faults are notorious for producing untoward healing.

Cracking of the cellophane happened once in the dressing of seventy clean wounds—hernioplasties, abdominal incisions, and wounds on the

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extremities dressed with the material of the proper thickness. In this instance it occurred on the fourth day after an appendectomy in a young boy 6 years of age. The wound healed per primam, however, in spite of this accident. No other difficulties were encountered with other children. However, before the No. 600 grade was used, cracking occurred too frequently in a small series of wounds dressed with thin wrapping cellophane. Obviously, therefore, just any sheet of cellophane cannot be used. With the thin variety, it was noted that the rectangle should not be cut excessively large, for large sheets cracked more readily than smaller ones, and that crinkling caused cracking. We advise that the material be autoclaved, for sterilizing by antiseptics or by boiling causes crinkling. Assurance may be given that if the No. 600 grade cellophane cracks, the break will occur at such a time that the wound will not become infected. Sheets of this thickness have been left on the abdomen as long as ten days without cracking. Moreover, a break will seldom occur before the fourth or fifth day of healing, and, if it does, Du Mortier[2] has shown that after this interval there is very little possibility of infecting the wound by external contamination. In fact, none of the wounds dressed with the thin cellophane which cracked on the third and fourth days developed an infection, nor have we encountered an infection or stitch abscess which properly could be attributed to the use of cellophane. We believe it is in every way an economical and satisfactory dressing for the clean wound.

For some time Hazen, of Washington, D. C., has covered wet dressings used on ambulatory patients with cellophane, fastened by adhesive borders to prevent soiling. They stay wet for a long period of time and cellophane is less expensive than oiled silk.

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A NEW COLOSTOMY SPUR-CRUSHING CLAMP*

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THE recent more extended use of modifications of the original Mikulicz operation for carcinoma of the colon has increased the need for an efficient spur-crushing clamp. As far as I am able to determine from conversations with other surgeons doing a large amount of colonic surgery, the crushing of a colostomy spur has heretofore been attended by considerable inconvenience both to patient and surgeon. While there are many such clamps on the market today, only one has given some degree of satisfaction. I refer to the clamp devised by Stetten. But even this instrument has not been uniformly successful in our hands. Among the difficulties that have

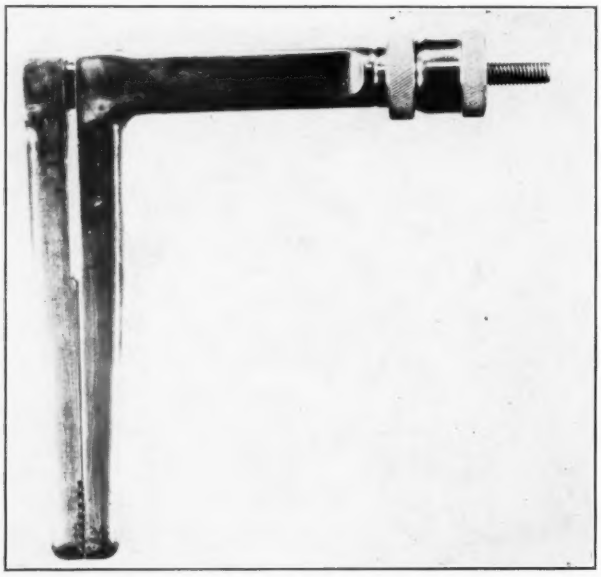

Fig. 1.—Photograph of the clamp with the blades closed.

been encountered may be mentioned: (1) slipping of the clamp; (2) the unusually long time required for complete crushing of the spur; (3) projection of the clamp beyond the surface of the skin, necessitating, in most instances, confinement to bed; and (4) the unusually wide blades of the clamp which make application of the instrument difficult in cases presenting small colostomy openings.

After considerable experimentation, the clamp pictured in the accompanying illustrations was constructed. It will be noted that the

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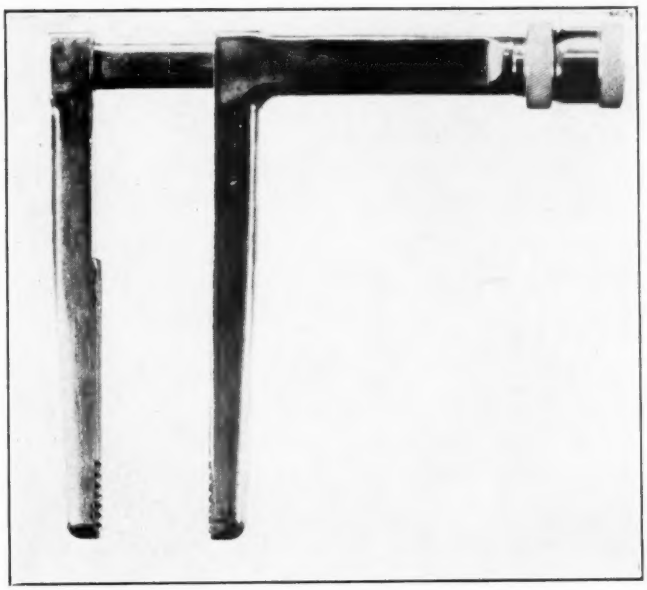

Fig. 2.—Clamp with blades opened. The instrument can be taken apart completely. It is important to cleanse and oil the smaller horizontal arm, in order to prevent rusting of the telescoping portion of the clamp.

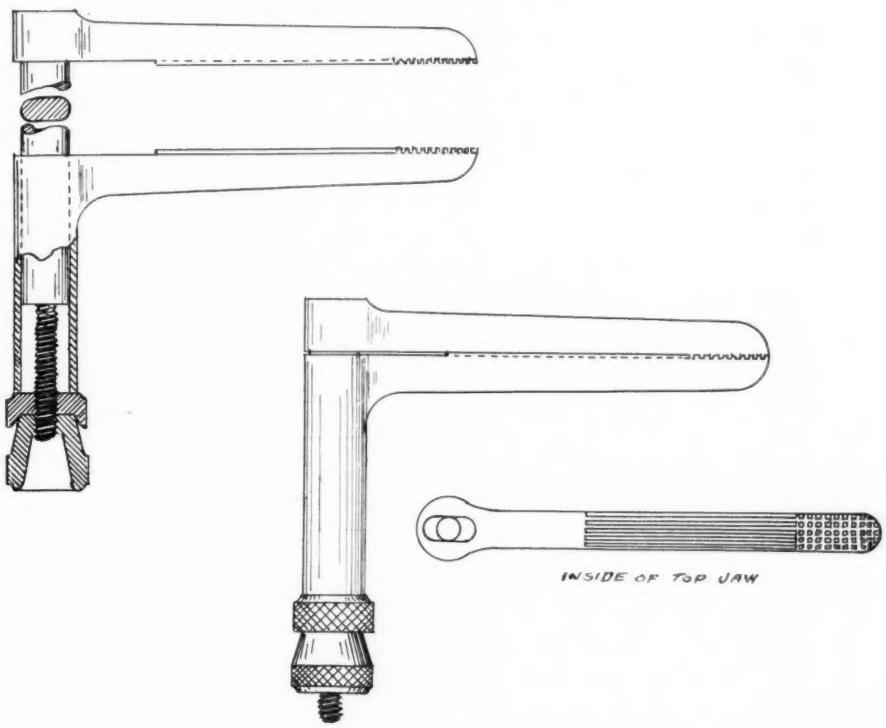

Fig. 3.—Diagrammatic representation of the clamp showing the finer details of construction.

instrument is right angled. Because of this, the distribution of the force of compression of the crushing blades is greatly increased and, at the same time, separation of the blades with slipping of the clamp cannot take place. Because the instrument is right angled, it does not project too far from the skin surface, thus allowing the patient to be ambulatory. The alternate grooves and projections on the visceral surface of each blade fit accurately into similar configurations on the opposite blade. This prevents slipping of the clamp. To accommodate patients with thin abdominal walls, I have had a smaller clamp constructed with shorter vertical blades. The efficiency of the clamp has not been impaired thereby.

Sufficient use of the clamp has been made to date to warrant recording our experiences with it. In each instance in which the clamp was used, the spur was crushed after a single application in a surprisingly short time and with little discomfort to the patient. The shortest time was 40 hours and the longest 78 hours. It must be emphasized that the turnscrews should be tightened every twelve hours in order to obtain maximum effect. In no case did the clamp slip off the spur, once it was applied.

*This clamp was constructed by B. Dubi, 555 Glenmore Ave., Brooklyn, N. Y., and may be obtained from the Kny-Scheerer Corporation of New York.

A CLAMP AND SPUR CRUSHER FOR OBSTRUCTIVE COLONIC RESECTION*

ARTHUR S. W. TOUROFF, B.S., M.D., NEW YORK, N. Y.

FROM time to time, surgeons have expressed dissatisfaction with the intestinal clamps and spur crushers commonly employed in performing so-called obstructive resection of the colon. The common criticisms have been that the clamps which are most effective are heavy and have rather long handles; and also that they require voluminous dressings to pad them and steady them in place upon the abdomen after operation. The objections to the spur crushers have been that they frequently slip off the spur, have insufficient crushing power, and also require large dressings to steady them. With the object of eliminating these various undesirable features, I have designed an instrument which, in actual practice, has fulfilled its purpose. The device consists of two units, a resecting clamp and a spur crusher.

The resecting clamp is of the well-known three-bladed variety, but its design differs considerably from that of conventional instruments. The central blade is stationary and is joined to the midpoints of two parallel side bars, the resulting frame being shaped like the letter H (Fig. 1). The two outside blades of the clamp are movable, and, instead of being hinged, slide back and forth upon the side bars, parallel to the stationary central blade. The ends of the movable blades are held in contact with the side bars by encircling collars. The position of each blade is maintained automatically by ratchets which engage in notches in the side bars and can be locked by small thumbscrews. Transverse serrations, scored on the apposing surfaces of the blades, tend to prevent the bowel from slipping from the grasp of the clamp. With the usual type of clamp, slipping of the bowel not infrequently occurs after the latter has become thinned out as the result of pressure applied over a period of several days. This slipping is due to the fact that, once the clamp is applied, no provision exists for taking up the slack between the blades and the thinned-out bowel. In the present device a spring mechanism, incorporated in each of the movable blades, takes up slack and causes the bowel to be gripped firmly at all times.

The spur-crushing unit is a modification of an instrument devised by Dr. DeWitt Stetten, to whom acknowledgment hereby is made. It consists of a short, powerful, two-bladed clamp which is tightened by a bolt situated at its upper end (Fig. 2). Transverse serrations, scored on the back of each blade, interlock with the serrations on the blades of the

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resecting clamp already mentioned. In crushing the spur, the resecting unit is employed in conjunction with the spur-crushing clamp in order to increase the crushing force of the latter, to stabilize it, and to afford a means of fixing it to the abdomen (Fig. 3).

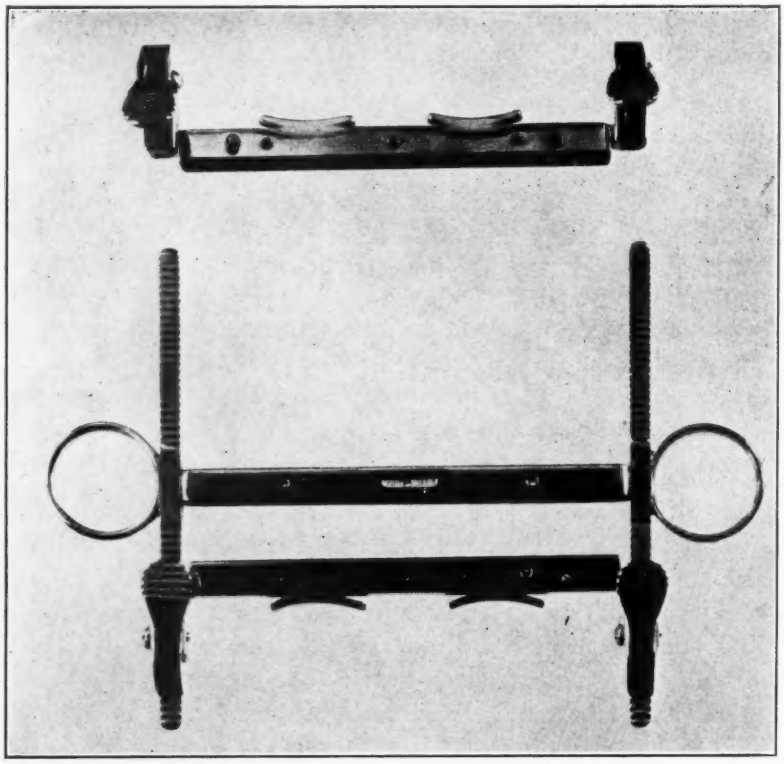

Fig. 1.—Resecting clamp, consisting of stationary central blade and two movable blades.

Note that central blade is part of an H-shaped frame. Lower half of clamp is partially closed. Note ratchets holding movable blade in place. The upper movable blade has been removed. Note grips for index fingers on frame, and thumbrests on movable blades. Spring mechanism incorporated in movable blades exerts continuous pressure on bowel when clamp is closed. (Thumbscrews which lock ratchets are not shown.)

In performing obstructive resection with these instruments, the tumor-bearing segment of bowel is isolated, an opening made in its mesentery, and the bowel freed of its blood supply in the usual manner. The two movable blades of the resecting clamp are removed, and the central blade is slipped through the opening in the mesentery beneath the isolated loop (Fig. 4, *1*).* The movable blades then are replaced and the two limbs of the isolated bowel clamped successively at the desired points. The surgeon does this by hooking his index fingers into the loops attached to the frame and forcing the movable blade nearest him toward the central blade with both thumbs (Fig. 4, *2*). As the movable blade advances, it is prevented from slipping backward by the auto-

*The author is indebted to Dr. Amiel Glass for the sketches comprising Fig. 4.

matically acting ratchets mentioned previously. After the first limb of the loop has been clamped securely, the maneuver is repeated and the opposite half of the clamp closed on the remaining limb. Usually this is best done by an assistant on the opposite side of the operating table, for he can exert stronger pressure and therefore close the remaining open half of the clamp more securely than can the surgeon from his side of the table (Fig. 4, *3*). The thumbscrews on the ratchet handles next are tightened, thus securely locking the blades in position. The tumor-

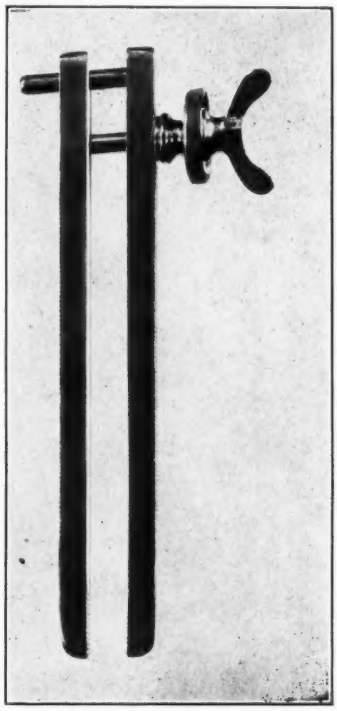

Fig. 2.—Spur crusher consists of a two-bladed clamp, closed by a bolt and locked by a wing nut. Note serrations (seen indistinctly) on the back of each blade. These interlock with serrations on the apposing surfaces of the blades of the resecting clamp. (Serrations on both instruments are best shown in Fig. 3.)

bearing loop of bowel then is resected with the cautery or carbolic knife. The choice of whether to suture the two limbs before or after resection, or not at all, rests with the surgeon. A split piece of gauze is placed beneath the instrument and the latter fixed to the abdomen by double tapes attached to Montgomery straps, one on each side of the abdomen (Fig. 4, *4*). These tapes are tied to the metal loops of the frame. The exposed bowel finally is covered with vaselinized gauze and a light dressing. The bowel is inspected daily and if the clamp at any time appears too loose, it may be tightened as much as desired.

After the desired number of days has elapsed, the afferent limb is released by opening the upper half of the clamp. If this limb is short and under tension and there is fear that the unclamped bowel may

retract into the abdomen, a series of sutures are passed through the edges of the open bowel and tied to the central (stationary) blade and the open movable blade (Fig. 4, *5*). Since the clamp still is fastened to the abdomen and the lower (efferent) limb still is gripped securely by the lower half of the clamp, the instrument serves as a fixed point to which the open bowel may be anchored. During the period in which the instrument remains in place, while the upper limb is draining, the local area and the instrument may be kept reasonably clean by gently irrigating with a bulb syringe each time the dressings are changed.

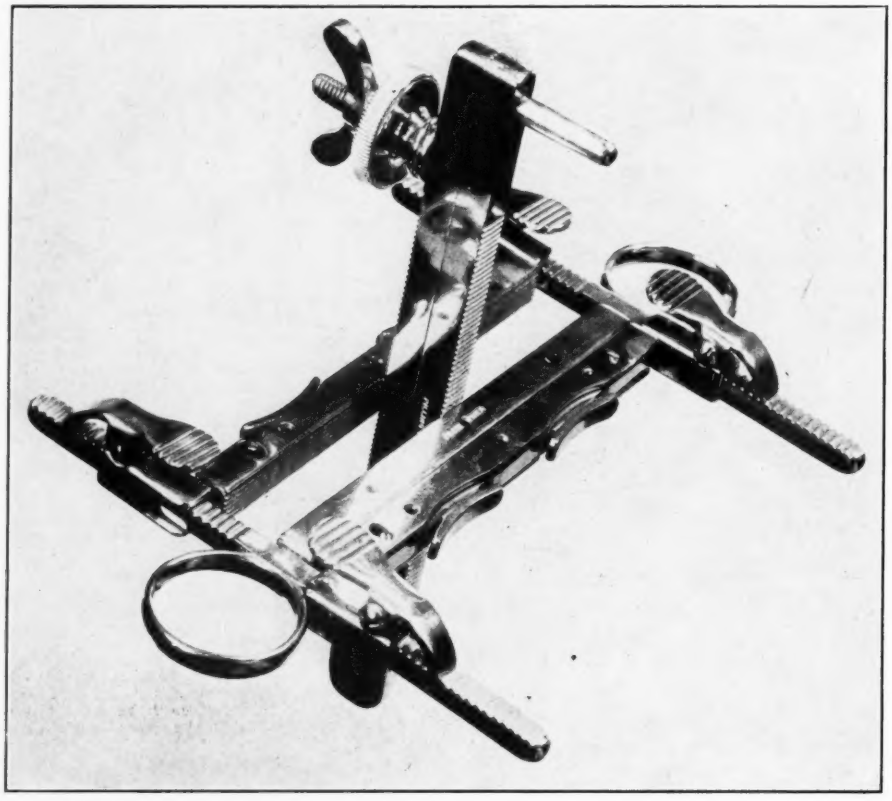

Fig. 3.—Crusher and resecting clamp assembled. After spur has been grasped by the crusher, the latter in turn is gripped between the central and one of the movable blades of the resecting clamp. Resecting clamp is applied at a point as low on the crusher as possible.

When the spur is ready to be crushed, the resecting clamp, if still in place, is removed. The spur is grasped with two Allis clamps and drawn gently out of the wound. As an assistant draws upward on the Allis clamps, the spur-crushing clamp is applied and tightened moderately. The Allis clamps are removed and traction now is made on the spur-crushing clamp by the assistant, in order to bring as much of it as possible out of the wound. The next step consists in applying the resecting clamp over the lower end of the crushing clamp in such a manner

that the latter is firmly compressed between the central blade and one of the movable blades of the resecting clamp (Fig. 4, *6*). This is done while the assistant continues upward traction on the spur-crushing clamp, the resecting clamp being closed over the crusher at a point as low on the blades of the latter as possible. The serrations on the back of each crushing blade interlock with those on the blades of the resecting clamp, and the spur crusher thus is fixed securely. Increasingly firm, uniform pressure then is applied to the spur by alterately tightening the bolt at the upper end of the crushing clamp and slowly closing the resecting clamp which encircles the lower end of the crusher. In this manner as much crushing force as is desired can be applied to the spur. By exerting this additional direct pressure upon the lower ends of the

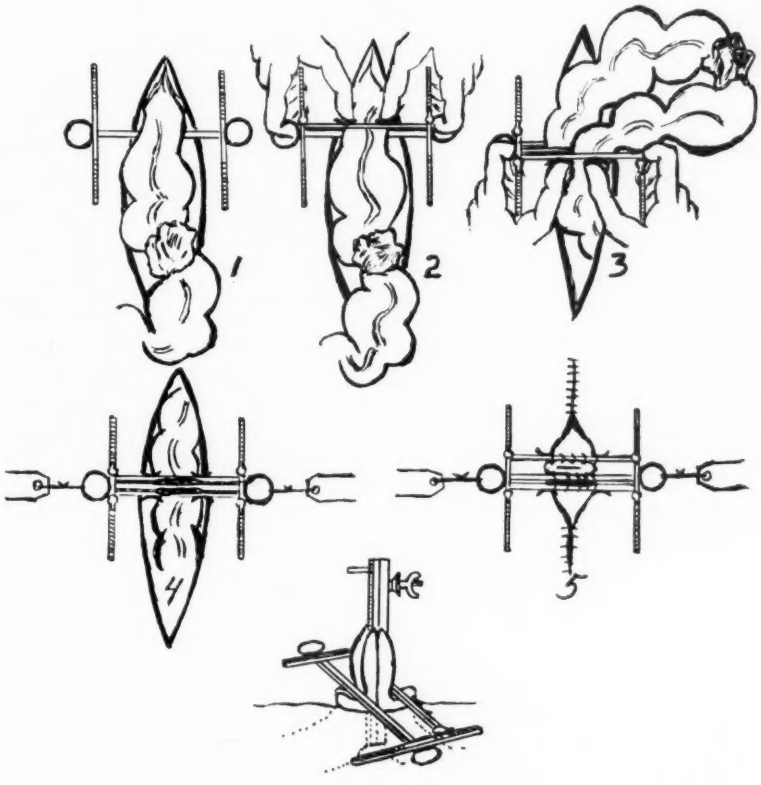

Fig. 4.—*1*, Tumor-bearing loop of bowel mobilized. Central blade placed beneath isolated loop, through the opening in the mesentery. *2*, Upper limb being clamped. Note direction of pressure of thumbs on upper movable blade. *3*, Upper limb has been clamped. Lower limb being clamped. (Note pressure again being made with thumbs, but this time from opposite direction.) *4*, Both limbs have been clamped and tumor-bearing loop of bowel resected. (Note instrument fixed to abdomen by tapes attached to Montgomery straps.) *5*, *Optional step:* After upper limb is unclamped, it may be anchored into wound by suturing it to the clamp. Lower limb may be kept clamped as long as desired. *6*, Spur crushing. Crusher has been applied to spur after the latter has been gently withdrawn from wound as far as possible. Resecting clamp then is applied to crusher to increase its power and permit fixation. Tapes of Montgomery straps (not shown in drawing) are attached to loops as shown in *4* and *5*.

crushing blades, the resecting clamp keeps the latter parallel to one another throughout their length. Thus, the tendency of the crusher to be wedged apart by the spur and to slip is reduced. After the resecting clamp has been closed as tightly as desired, the blades are locked by the thumbscrews, and the clamp is fixed to the abdomen by tapes attached to Montgomery straps as described previously. The spur crusher thus is immobilized. Finally, a split piece of gauze is placed beneath the resecting clamp and several split pads about the projecting spur crusher. Because of the firm immobilization of the crushing clamp, the patient may be gotten out of bed at once if desired. The crusher is tightened daily, by tightening the bolt at the upper end and further closing the blades of the resecting clamp at the lower end, until the spur is cut through. This usually requires four or five days.

The instrument,* which has been used with satisfactory results during the past eight months, possesses the following attributes: (1) It is of light weight and small size. (2) It has no long projecting handles. (3) Voluminous dressings are unnecessary. (4) The opened bowel may be anchored in the wound if desired. (5) Spur-crushing action is powerful and uniform. (6) The patient need not remain in bed while the spur is being crushed.

REFERENCE

Stetten, DeWitt: An Improved Colostomy Spur Crusher, Am. J. Surg. 4: 327-328, 1928.

*The instrument is made by the Geo. P. Pilling & Son Co., Philadelphia, Pa.

ACUTE INTESTINAL OBSTRUCTION CAUSED BY NONABSORBABLE SUTURE MATERIAL

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(From the Pember-Nuzum Clinic)

NO DOUBT, nonabsorbable suture material as a cause of intestinal obstruction is extremely rare. Greenhill[1] collected 109 cases of foreign bodies left in the abdomen after operation and in only one, a case reported by Eckstein[2] in 1926, was a knotted thread of sufficient importance to be noted. In this case the patient was admitted with a fistula which had developed after appendectomy performed in another clinic a year previously. Immediately after removal of a thread, 10 to 20 cm. long, the fistula closed.

It is interesting to note in the review of the literature that Cassuto[3] in 1934 reported five cases in which nonabsorbable suture material had penetrated the bladder and calculus formation had taken place on the loop of the suture material. In each case it was possible to remove the calculus along with the piece of thread. It was his suggestion that surgeons guard against placing stitches and sutures in proximity with the posterior wall of the bladder and that they use the method suggested by Pestalozza, in which a good portion of the peritoneum is dissected anteriorly above the upper strait of the uterus isolating the peritoneum without exposing the bladder. This procedure facilitates a good peritonization of the stump or a correct fixation of the uterus according to the case.

Fenkner[4] reports a case in which one and one-half years after gastroenterostomy a second operation was done for a supposed marginal ulcer. Excision of a segment of small intestine and fragment of gastric wall was performed. A double silk suture lay about the gastrointestinal opening and in two directly opposite places protruded through the mucosa into the lumen of the small intestine in such a way that it could be moved back and forth, thus causing continuous irritation.

Fredet,[5] discussing stenosing cancer of the small intestine and granulomas due to foreign bodies, reports a patient who had been operated upon seven and one-half years before for carcinoma; 30 cm. of small intestine had been resected. After this period of time, the patient developed indications of stenosis of the end of the small intestine; on reopening the abdomen, it was found that there was an unrecognized appendicitis of long standing. The surgeon took advantage of the opportunity to inspect the condition of the suture of the small intestine and found the intestinal continuity perfect, but for a distance of a few centimeters above and below there were small, whitish lenticular patches

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3 to 4 mm. in diameter inserted between the peritoneum and the muscular layer. Four of these were removed and examined histologically and were found to be granulomas due to foreign bodies. Numerous plasmodia were seen containing the debris of linen thread.

Ponomarev,[6] in his article concerning the foreign bodies left in the abdominal cavity after laparotomies, reports two cases from his own observation together with a brief review of the literature. He gives Albitzky's* series of cases which number 315 reported up to 1917; of these foreign bodies, thirteen cases were ligatures. In conclusion, the author mentions briefly several other cases which seemingly have not been reported. When the author reported the first case in a local meeting of physicians (Tomsk province), two other men reported similar cases in the open forum discussion which followed. One of these cases disclosed at autopsy a piece of omentum with ligature in the abdominal cavity of a woman who died after operation (reported by Beigel).

Doubrere,[7] in the discussion which precedes the case histories, does not refer to occlusion due to aberrant silk sutures, but lists under causes of mechanical obstruction tampons and other such objects left in the abdominal cavity. In one case which he cites, occlusion was due to an extra catgut suture which fastened the iliac S to the bladder and produced a kink in the sigmoid. Removal of this stitch on the third day after the original operation relieved the occlusion with almost normal postoperative course. On the tenth day after the second operation, there was some urinary retention and hemorrhagic cystitis.

While this discussion deals primarily with nonabsorbable sutures, some rather interesting reports of complications following the use of absorbable sutures were found.

Fiolle and Hayem[8] reported two cases of intestinal occlusion following appendectomy. Exploration in the first case revealed a loop of small intestine twisted and adherent to the site of the recently removed appendix. A second case had a threatened obstruction soon after removal of a ruptured appendix. However, symptoms disappeared after two weeks. Three years later occlusion occurred requiring intervention. At this time a long fibrous frenum was found extending from the stump of the appendix to the small intestine which was bent into a V at this point by traction of the frenum.

In the discussion following, Alglave also mentioned a case of occlusion following appendectomy, the adhesion being an epiploic frenum from the appendix stump to the small intestine. The conclusion in these cases was that the adhesions were the result of not burying the stump and they attached no significance to the possibility that allergy to the catgut used in tying of the stump might be a factor in causing the adhesions. However, Gilson and Gratia[9] conducted a series of experiments on guinea pigs which proves conclusively that the Arthus phenomenon

*This article could not be located.

may be provoked in sensitized organisms by catgut, which, as a sheep product, is an antigen. An allergy to catgut may be produced by catgut sutures used in a previous operation, so that reactions, which even may include intestinal occlusion, may develop in a later operation. The three cases of occlusion just mentioned in which the occlusion was due to frena arising from the site of the previous operation are quoted from the literature. The authors experimented with a desensitizing treatment of injections to be administered before undergoing operation and found it successful in overcoming this allergy and consequent formation of frena.

Urban,[10] reporting a rare case of ileus in 1929, cited a patient, a domestic, 20 years of age, who was admitted to his clinic Sept. 5. She had the appearance of being extremely ill. The abdomen showed an operative scar in the middle region and another at the right side. The abdomen was not particularly distended and was only moderately sensitive to pressure. The major pains were localized in the right lumbar region and here also there seemed to be greater painfulness to pressure. The abdominal walls were tense. Early on Sept. 6, there was recurrence of severe pain. The abdomen became more and more distended and tense. When the position of the patient was changed, there was distinct dullness in the dependent portions. The rest of the abdomen was tympanitic. The hepatic dullness had practically disappeared. Deep palpation was not possible because of the great tension of the abdominal walls. Temperature was 37.2°; pulse, 96 and small.

When asked for the history, the patient reported that in April, 1927, she had undergone an operation in a gynecologic clinic because of menorrhagia. Further inquiry revealed that the operation had consisted of extirpation of the right adnexa, the left tube, and wedge excision from the left ovary.

On Nov. 29, 1927, the patient underwent another operation because of violent pain in the right lower abdomen. Numerous strands of adhesions were found in the ileocecal region and they were severed. The appendix was not found, but there was a small stump at the site of its probable origin. It would seem, therefore, that the appendix was removed at the time of the gynecologic examination.

After that operation, the patient was free from symptoms until Sept. 3, 1928. On that day, according to the report, abdominal pain and vomiting set in after the patient had partaken of pears and beer.

On September 6, operation was performed under ether and oxygen anesthesia. When the abdominal cavity was opened, there were found generous quantities of malodorous, black liquid. The loops of the intestine were very much distended and showed black discoloration. The distended snarl of intestine was lifted out and it was found that it was a matter of extensive incarceration of the ileum as far as Bauhin's valve. The mesentery belonging to the darkly discolored intestinal loop was ligated by a free loop of silk thread with a lumen which barely admitted one finger. This ligation had induced total gangrene of the corresponding portion of the ileum. The condition of the patient was so poor that it was necessary to terminate the operation quickly. For this reason, the gangrenous loops of the intestine were resected, the two stumps were drawn into the upper angle of the wound and sutured, and the rest of the abdominal cavity was closed after argochrome had been poured in. The resected portion of intestine measured 70 cm. in length.

After a stormy convalescence, the patient recovered. Urban succeeded after several months in closing the fistula by means of a submerged intestinal tube.

Urban attempts to explain how a free silk ligature could induce ileus. One explanation seems to lie in the assumption that one of the ligatures

applied for submersion of the stump of the tube at the time of the gynecologic operation mentioned above became partially loosened for some reason and protruded into the free abdominal cavity with the major portion of its lumen. Ligatures on the suspensory ligaments of the uterus or ligatures around a point in this region would also correspond, as to lumen, to the incarcerating ligature which was found. Now a loop of intestine seems to have become entangled in this loose silk ligature. Due to peristalsis, more and more intestinal loops were forced into this ligating thread, until the continued intestinal movements pulled the ligature from its original site of attachment. The distended intestinal loops were unable to extricate themselves from the constricting thread and complete incarceration was the result.

In conclusion, he says that, even though the most varied and peculiar causes for intestinal occlusion have been reported, the literature does not seem to contain a case similar to the above, with free silk ligature forming a stricture around a portion of the small intestine, binding it so tightly that grave ileus and complete gangrene of 70 cm. of intestine ensued.

I wish to report a similar case which recently came under my care.

A doctor's mother, Mrs. C. M., aged 71 years, married for forty-nine years, entered Mercy Hospital, March 6, 1938, with acute intestinal obstruction and chronic arthritis. Her husband was in the hospital at the same time for urinary obstruction. The patient had suffered from arthritis for a period of thirty years. She had had a hysterectomy performed twenty-four years before. She had had no loss of weight in the last year or two, though appetite had been poor for the last year. Bowels had been looser for the past year; she had dark stools only when she took cathartics; normal consistency was thinner than gravy. She complained of no excessive flatulence. She had noticed abdominal enlargement for the last two years, but had never mentioned this to anyone. The menopause was passed in 1914 when the operation was performed.

Her chief complaint was a dull pain in the abdomen. She felt quite well up to Monday, Feb. 28, when she had a normal bowel movement. Tuesday she had marked anorexia. Thursday and Friday she vomited and the vomitus was heavy brown material; several enemas were given with no result and nothing was passed per rectum since Monday. Patient's temperature was 99°; pulse, 95; respiration, 20. Her height was 5 feet, 2 inches; weight, 110 pounds.

General appearance showed senile nutritional changes comparable with age. She had a mild pallor skin; bilateral arcus senilis, pupils normal; artificial dentures; chest normal; senile emphysematous changes. Heart was normal and regular; blood pressure, 160 systolic and 80 diastolic. The abdomen was distended with the skin surface shiny; outline of distended bowel in right lower quadrant and midline. Borborygmus and tinkling were most marked in right upper quadrant. Extremities, i.e., knees, elbows, and hands, showed arthritic changes; atrophy of the muscle groups, upper arm, forearm, hands, calves, and thigh. Pelvis was negative; reflexes impaired.

Tentative diagnosis was (1) acute intestinal obstruction, probably on the basis of malignancy; (2) infectious arthritis; (3) multiple ankylosis; (4) edentulous and artificial dentures; (5) senility and arteriosclerosis. Laboratory findings at this time showed urine with a specific gravity of 1.031, trace of albumin, three plus sugar, and one plus acetone, also occasional pus cells. Blood count revealed 93 per

cent hemoglobin, 4,410,000 erythrocytes, and 8,600 leucocytes. Wassermann test was negative. A scout film showed marked distention of the small bowel in stepladder arrangement. The duodenal tube (Fig. 1) was introduced with considerable difficulty and x-ray check-up following aspiration showed less distention with arrangement of the distended loops less pronounced. The duodenal tube was apparently extending into the duodenum. Operation was deferred to allow the patient's son to arrive; her general condition was improving. On March 6, she was given 35 c.c. of 15 per cent sodium chloride intravenously. On March 8, fluoroscopic examination of the colon was ordered. During the administration of a barium enema, the x-ray

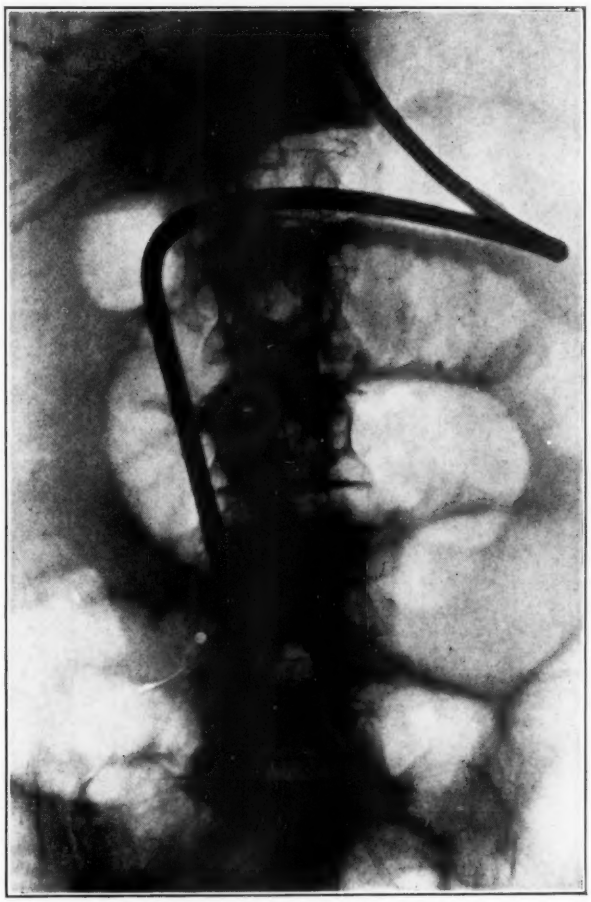


Fig. 1.—Loops of dilated small intestine with the duodenal tube in place.

(Fig. 2) showed the barium entering the colon freely until it reached the midportion of the transverse colon, at which point the barium hesitated and considerable backward pressure was established before the barium passed this point. It was impossible to milk the barium past this point by palpation for a time, and then considerable barium passed into the cecum. Films taken after fluoroscopy confirm the above findings.

Following the barium enema on March 8, at 10:05 A.M., the patient was taken into the operating room. Under local anesthesia, a small lower right oblique incision was made over the most prominent loop of intestine. On opening the peritoneum, a large amount of straw-colored fluid escaped. Exploring with one finger, an in-

durated loop of bowel was brought up which had a proximal dilated loop, a distal collapsed loop, and a dilated loop about 10 cm. in length which was constricted between these two loops of bowel. On first examination, this appeared like an infiltrating lesion on the mesenteric side, but further inspection showed this to be a single strand which looked like silk or linen tied around this small loop of intestine (Fig. 3).

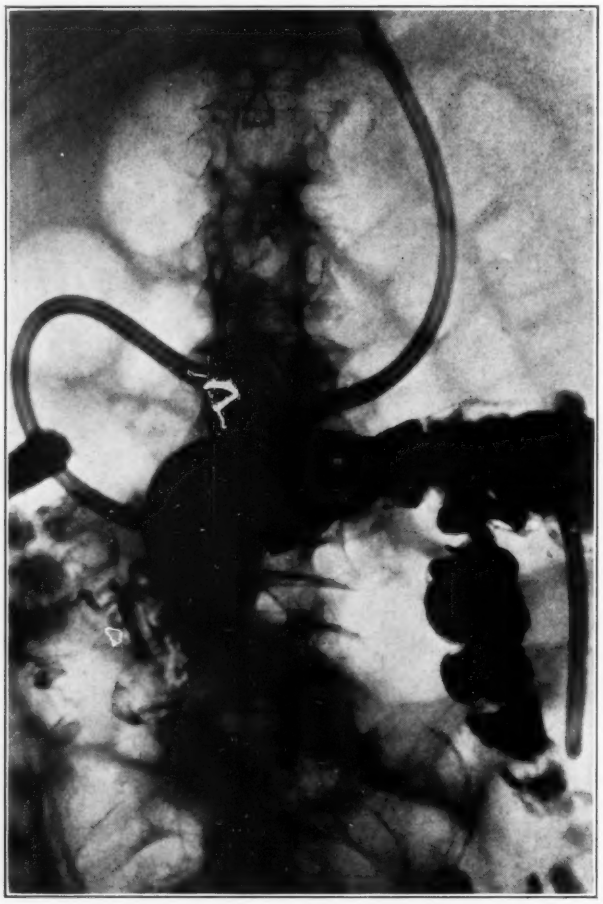


Fig. 2.—Loops of dilated intestine with the duodenal tube and colon filled with barium.

The strand was cut and removed, and after its removal, the bowel straightened out and started to function. A constricted area was left on either side with a lumen large enough to insert the end of the finger. With the return of peristalsis through the constricted areas and filling of the distal collapsed portion, the bowel was returned to the abdomen and the wound was closed.

The following day the patient was given 400 c.c. of citrated blood. She made a very uneventful recovery. The patient was discharged from the hospital March 18 and has been entirely well as far as her intestinal condition was concerned. She has had a rather marked improvement in her arthritis.

Following this unusual experience, I wrote to the surgeon who had operated upon her twenty-four years previously. He stated that at that time he was working in a sanitarium which he left in 1918. The institution had been sold three times since then and the last superintend-

ent, in cleaning up and transferring things to another institution, had burned much of the material, which he considered junk, but which proved to be all the surgical records and records of the nurses' training school; this incident had caused him no end of embarrassment. He could not recollect the patient nor the procedure carried out, but he

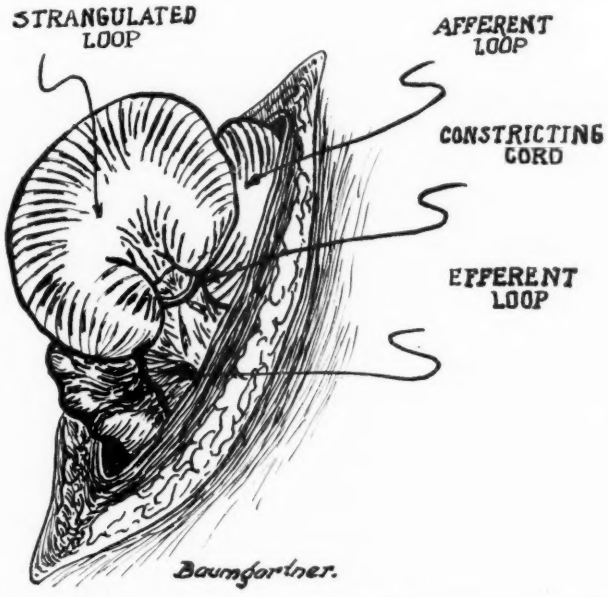
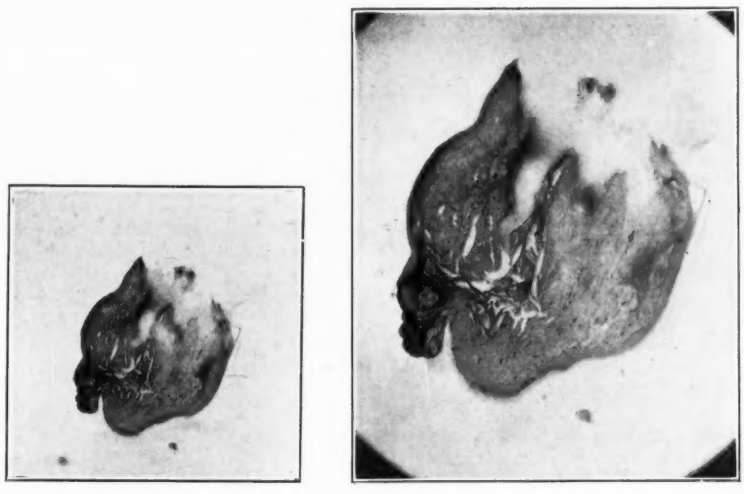


Fig. 3.—Showing loop of obstructed small intestine delivered through incision.



A. *B.*

Fig. 4.—Photomicrograph. *A*, Enlarged 60 times; *B*, enlarged 120 times.

stated that he had never, in all his surgical experience, used anything but catgut and silk inside the abdomen. He raised the question as to whether this could not have been a fibrous band rather than a suture.

The material was turned over to the Pathological Section of the Wisconsin State Laboratory of Hygiene, and the report stated that the

section examined was typically that of suture material. Photomicrographs were made of the sections (Fig. 4). *A* is enlarged 60 times and *B*, 120 times.

The explanation given by Urban appears logical to me. From the history, it would seem that this suture had produced partial obstruction in this patient over quite a long period of time, and finally the bowel had worked all the way through the loop to make the obstruction complete. The fact that the bowel straightened out so completely after the ligature was cut showed that the condition encountered was of recent origin. Before operating upon this patient, we checked what appeared to be the most distal and dilated loop of the bowel that showed in the x-ray film and on physical examination. Drainage of this loop by enterostomy was contemplated, having the idea of malignancy firmly fixed in mind. The area was explored with the finger and naturally it was a great surprise to be able to deliver the lesion through such a small opening.

Apparently this happens so seldom that the reporting of this case is of very little importance except as a surgical rarity. During a recent visit to eastern clinics where such large quantities of silk are used in the abdomen, I inquired of several surgeons if they had ever seen a like complication and none could recall such a case.

It is not my purpose to discuss in any way the relative merits of nonabsorbable or absorbable suture material in the abdomen, but simply to report a very interesting and rare case of intestinal obstruction caused by a piece of nonabsorbable suture material that had been introduced into the abdomen twenty-four years previously.

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Editorials

Intratracheal Suction in the Management of Postoperative Pulmonary Complications*

PULMONARY complications continue to be an important cause of morbidity and mortality following surgical operations involving especially the upper abdomen. As the incidence of complications has not decreased in proportion to improvements in anesthesia, a factor other than anesthesia therefore must be regarded as the causative agent in most cases in which the pulmonary lesions are not attributable to embolism or infarction. This factor is bronchial secretions.

Bronchial secretions, when present before operation, may consist merely of a small amount of mucoid material which is unnoticed by the patient and surgeon. If not present before operation, the secretions in the bronchi may occur from aspiration of pharyngeal secretions or from an increased production of mucus by the bronchial mucosal glands. If stasis of bronchial secretions is allowed postoperatively, the patient is subjected to a serious hazard, in that obstructing secretions within the tracheobronchial tree not only cause a decrease or loss of function of localized segments of the lungs but are particularly harmful in that they are infective secretions, usually containing pneumococci. Furthermore, the viscosity of the secretions makes voluntary evacuation a difficult problem for a weakened patient with a painful incision.

The diagnosis of retained secretions is aided by an appreciation of the significant symptoms and signs. The most important symptom is a relatively unproductive, wet, "rattly" cough, indicating that bronchial secretions are being incompletely evacuated. A wet cough which is productive of sputum and which is followed by a dry, unproductive cough signifies that secretions are temporarily being evacuated effectively. This sequence should warn the surgeon to provide for the evacuation of all secretions that subsequently occur. A sudden unexplained rise in temperature and in respiratory and pulse rates in the first several days after operation is also suggestive of retained secretions. The stethoscope is of greater aid than the roentgenogram in the early detection of secretions, in that rhonchi can be heard before the complications of the obstructing secretions that were causing the rhonchi can be seen with a roentgenogram. Rhonchi, rather than râles, are significant for an early diagnosis since râles are usually the late, or pneumonic, expression of secretions that were causing the rhonchi. Furthermore, rhonchi may be present when the cough is dry. Varying degrees of dullness,

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diminished breath sounds, and fremitus are usually present when the bronchial obstructive condition becomes more advanced. Tracheal râles and a wet type of breathing which is audible to the naked ear signify considerable retention of secretions. A portable roentgenogram is of value in determining the extent of parenchymal involvement. Although the roentgenogram will determine if atelectasis of one lobe or of one lung is present, the roentgenogram frequently fails in differentiating between lobular atelectasis and pneumonic infiltration. Frequently the conditions coexist, but, as treatment is designed to relieve the obstructing bronchial secretions which have been the causative agent, it is not of great therapeutic importance that a distinction be made.

The prophylaxis of nonembolic postoperative pulmonary complications is the prevention of retained secretions. The prevention of aspiration of pharyngeal secretions during and immediately following operation and the evacuation of bronchial secretions, whatever their etiology, are the most important prophylactic considerations. The factors which influence the aspiration of secretions are the type of anesthetic agent; the ease, depth, and length of anesthesia; the position of the patient during the operation; the duration of the unconscious period following operation; and the position of the patient during this period. The Trendelenburg position should be used whenever possible during the operation and until the patient regains consciousness.

The various measures which have been advocated in the prevention and treatment of nonembolic pulmonary complications are expressions of the fundamental importance of adequate bronchial drainage. As voluntary cough is the most important mechanism in the prevention of retained secretions, these measures should include, first of all, an appreciation by the patient, nurse, and surgeon of the periodic necessity of an effective cough to determine if and when secretions are present. The patient's cooperation should be obtained by explaining to him the reason for periodic coughing, even when coughing is accompanied by considerable pain. Furthermore, a painful incision may be supported by the nurse or surgeon or the patient may be shown how he can support the incision himself. When secretions are known to be present, the patient should especially be encouraged and assisted to cough fifteen minutes after each narcotic injection. Voluntary cough is more effective if the patient takes several deep breaths before each cough.

Other prophylactic and therapeutic measures include the use of the Trendelenburg position during the first twenty-four hours after operation unless this position interferes with the effectiveness of cough. In such instances the intermittent or constant elevation of the head of the bed is indicated. The frequent change of the patient from one lateral position to the other is of advantage in favoring bronchial drainage from the lower lobes, especially when the patient is in the Trendelenburg position or in a horizontal position. The patient should be en-

couraged to cough after each change of position. Hyperventilation with 15 per cent carbon dioxide in oxygen produces bronchial dilatation and is a valuable measure in certain cases. When unconsciousness is present, carbon dioxide should be given only when the patient is in a position which favors gravitation of secretions toward the oral pharynx where they can be aspirated. In a conscious patient carbon dioxide always should be followed by voluntary cough to determine if the tracheobronchial tree is dry and to promote evacuation of secretions should the cough be wet. Although failure of these measures may occur as a result of unconsciousness, more often it is due to the inability of a sick patient to cough effectively.

If the measures mentioned should fail to evacuate the secretions, they should be removed by intratracheal suction. The methods for providing suction are by bronchoscopy or by a catheter introduced into the trachea and bronchi. The effectiveness of the bronchoscope for the removal of postoperative bronchial secretions was first demonstrated in 1925 by Jackson and Lee and it has been of increasing usefulness in clinics in which a trained bronchoscopist is available. Bronchoscopy possesses the advantage of allowing actual visualization of the interior of the tracheobronchial tree and it enables one to be certain that all obstructing secretions have been removed. More recently the intratracheal catheter has been found to be a simple and effective means for removing secretions in the trachea and bronchi after operation. Catheter suction is a measure which is more readily available, requires less proficiency in administration, and is especially applicable when repeated aspirations at frequent intervals are required. We frequently employ catheter suction as the only means for providing intratracheal suction, but we have no hesitancy in using bronchoscopy in the occasional instance in which difficulty is encountered in introducing the catheter and in which there is uncertainty about the removal of all secretions by the catheter. Bronchoscopy, if expeditiously performed, is frequently less upsetting to a critically ill and cyanotic patient, as oxygen can be conveniently administered through the bronchoscope while the tracheobronchial tree is being cleared. In this type of case bronchoscopy may be used as the initial measure and catheter suction is then used for the repeated aspirations which are usually required in order to maintain adequate bronchial drainage until the patient is able to cough effectively.

The requirements for catheter suction are a No. 16 French soft rubber urethral catheter, a suction apparatus, and connecting tubing. A glass bronchoscopic collecting tube is customarily interposed in the system in order to estimate the amount and consistency of the secretions. The open end of the glass collecting tube is fitted with a rubber stopper with a one-quarter inch hole. As constant suction is too upsetting and provokes cyanosis, the suction is applied intermittently by occluding the hole in the stopper with the thumb. If a collecting tube is not used,

intermittent suction is obtained by alternately pinching and releasing the connecting tubing or by the use of a glass Y-tube in the system, the open arm of the Y being intermittently occluded with the finger. A pus trap should be employed to prevent the secretions from entering the suction apparatus.

The catheter is introduced into the nares without cocainization of the nose, throat, or trachea and is directed posteriorly until it touches the arytenoids. The catheter is then withdrawn slightly, the patient is asked to breathe deeply, and the catheter is quickly advanced into the trachea during deep inspiration. If the patient tends to swallow the catheter, the tongue should be held by the surgeon to prevent swallowing. The patient is then asked to breathe deeply and the catheter is again advanced during inspiration. If this maneuver should be unsuccessful, the patient is asked to cough and the catheter is advanced during the inspiration following it. Should the cough reflex be absent in an unconscious patient, it can usually be stimulated by turning on the suction when the catheter is at the level of the larynx. Otherwise, the suction is not applied until the catheter has been introduced into the trachea. The tracheal secretions are aspirated before advancing the catheter into the main bronchi. As the use of the suction provokes severe coughing, the amount of suction should be regulated and the suction should be applied only for periods of several seconds each, the patient being allowed to take a few deep breaths between each application of the suction. Actually the coughing which accompanies the procedure is advantageous in that it displaces considerable bronchial secretion into the trachea where it is removed before the catheter is advanced to the level of the bronchi. The catheter is introduced into the right bronchus without difficulty; in order to introduce it into the left bronchial tree, the catheter is withdrawn into the trachea and the patient's chin is rotated far to the right side before the catheter is advanced. When the tip of the catheter has reached the level of the orifice of the lower lobe bronchus, the outer end of the catheter will be about three inches from the external nares. If the physical or roentgenographic examination shows a greater involvement on one side, the patient may be rolled on the contralateral side during aspiration of the more involved lung. Posture will thereby aid the cough in evacuating the secretions from the smaller bronchi so that they can be removed from the main bronchi. The duration of the aspiration is usually one or two minutes, the aspiration being continued until the tracheobronchial tree is dry.

The secretions obtained by intratracheal suction are invariably thick and tenacious. The bronchial obstruction in atelectasis, when observed bronchoscopically, is usually due to a diffuse accumulation of thick secretions rather than to a strictly localized mucoid plug. The general improvement of the patient following removal of obstructing bronchial secretions, the relief of dyspnea, the disappearance of cyanosis, and the

cessation of the constant, wearing, relatively unproductive wet cough are usually rapid and at times dramatic in their suddenness. An appreciation of the above conception of the causative mechanism of nonembolic pulmonary complications and the more frequent use of the prophylactic and therapeutic measures outlined will greatly reduce the postoperative morbidity and mortality due to respiratory complications.

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Correct Speech

A DOCTOR'S degree should be a mark of distinction of a learned individual. Indeed, a doctor's degree, with the possible exception of Doctor of Medicine, always indicates the acquirement of knowledge and carries with it the implication that one is able to transmit that knowledge in a creditable manner. Unfortunately, too many physicians, although they have doctor's degrees, pay little or no attention to correct speaking, because they apparently have the idea that their sole obligation to society is administration to the sick and that there is little need for transmitting their ideas in a correct manner. This statement may seem a little harsh and is undoubtedly so, because even the physician who is most careless in his speech is usually not slovenly but disregards the niceties of the English language in speaking and writing. The fault for carelessness in speech lies not with the men themselves, I believe, but in the training which they have received in medical school. I am sure that if adequate emphasis were placed on the necessity of correct speech during a student's medical school days physicians would have little difficulty in speaking correctly. Too frequently a physician in discussing an esophageal lesion will refer to "my" or "your" esophagus and in discussing the symptomatology will say "you" have dysphagia. Although the use of the personal pronoun apparently may emphasize a point, it is incorrect; and, at times it is even quite ludicrous. I recall several years ago listening to a presentation on vulvectomy in which the essayist described, by means of photographs, the operative technique. The patients illustrated were all negresses. In the final step of the operation, the essayist showed how a perivulvar cutaneous flap was sutured to the anal rectal mucosa. With the picture of a negress on the screen, the essayist proudly stated to the audience: "Now I take this cutaneous flap and suture it to my anal rectal mucosa." One wondered how he would get himself out of such a difficulty into which he had gotten so easily.

Another commonly made mistake is the incorrect use of the word "temperature." All objects have temperature, whether animate or inanimate. Whereas during life the temperature of the human body is

dependent upon intrinsic heat production and external radiation, after death the temperature of the body becomes that of the surrounding medium. Under normal conditions, the body temperature is 98.6° F. There may be deviations from this normal temperature in that it may be above or below normal. When the temperature is above normal, the individual has fever or has an elevated temperature. However, there is the apparent conception that the use of the term "temperature" for "fever" is somewhat nicer and does not denote as severe a reaction. I have the impression that many prefer to use the word "temperature" when there is only a slight pyrexia and to use the term "fever" when there is a hyperpyrexia. A frequently made mistake is the use of the word "operate" as a transitive verb. Whereas it is possible for a psychiatrist who has hypnotized a patient to operate that patient very much as one could a mechanical monkey, a surgeon operates upon an individual and does not operate him. A frequent error which is more likely to be made by nurses than physicians is the use of the word "hemorrhage" as a verb rather than as a noun, apparently because "bleeding" is considered somewhat vulgar. Whereas one cannot deny that bleeding in most instances is extremely undesirable, it can hardly be considered vulgar or common. Frequently there appears in the nurse's notes of a patient's chart, a statement that the patient "hemorrhaged" rather than that the patient bled. As hemorrhage is a noun, it is not possible for one "to hemorrhage," but one may have a hemorrhage or may bleed. Very frequently made mistakes are the uses of the names of certain diagnostic instruments as verbs. So frequently is this done that they have become almost correct by right of usage; as examples, "to cystoscope," "to proctoscope," or "to gastroscope" a patient. A cystoscope, a proctoscope, and a gastroscope are instruments of diagnosis and the respective methods of examination are cystoscopy, proctoscopy, and gastroscopy. It is possible to perform these diagnostic procedures, but one should not use the name of the instrument as a verb. Instead of saying that the patient was cystoscoped, it should be stated that a cystoscopy was done, or a cystoscopic examination was performed.

Probably one of the most frequently made mistakes is the use of the adjective "tubercular" for infections produced by the tubercle bacillus. "Tubercular" denotes morphology and is descriptive of lesions which are nodular and its use should not be limited to lesions produced by the tubercle bacillus. Whereas an infection produced by the tubercle bacillus is a tubercular one in that tubercles or nodules are formed, it is equally as true that other granulomatous lesions, such as actinomycosis or leprosy, are tubercular infections. If one wants to designate an infection as being caused by the tubercle bacillus, one should use the adjective referring only to such a lesion, calling it a tuberculous one. Apparently the adjective "tubercular" is thought to denote a less severe infection than a tuberculous one. Whereas a tubercular infection is one in which

the lesion is nodular, the term referring to the morphology of the condition, a tuberculous infection is one which is produced by tubercle bacillus.

Whereas these errors in speech may seem of little consequence and of little importance during the daily work of a busy practitioner, they represent a failure to pay attention to details which frequently is of so much importance to a physician. It is only by being meticulous in details that we, as physicians, will be able to do our best work. In addition to this, it should be the obligation of a physician to uphold the dignity of the profession not only by practicing medicine in the best way he can, but also by being worthy of his doctorate in every sense of the word.

—*Alton Ochsner.*

Erratum

In the article by Emanuel B. Kaplan entitled "Pathology and Operative Correction of Finger Deformities Due to Injuries and Contractures of the Extensor Digitorum Tendon," appearing in the July issue of the JOURNAL, in Fig. 1 on page 37 under the caption "insertions of inteross." within the illustration, the lower longer line, instead of pointing to the insertion of the interosseous on the other side, incorrectly points to the insertion of the extensor tendon at the base of the proximal phalanx.

Recent Advances in Surgery

CONDUCTED BY ALFRED BLALOCK, M.D.

THE ESSENTIAL NATURE OF NONSPECIFIC GRANULOMATOUS LESIONS OF THE GASTROINTESTINAL TRACT

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(*Continued from the August issue*)

THE RELATIONSHIP OF NONSPECIFIC GRANULOMATOUS LESIONS OF THE ALIMENTARY TRACT TO THE ABDOMINAL LYMPHATIC SYSTEM

1. *The Relationship of Nonspecific Granuloma of the Alimentary Tract to the Solitary and Aggregated Collections of Lymphadenoid Tissue Contained Therein.*—Lymphadenoid tissue is constantly and characteristically found distributed throughout the wall of the alimentary tract in greater or lesser amount. Undifferentiated collections of this tissue are found irregularly distributed between areas in which the lymphadenoid tissue takes on an added importance because of the developmental augmentation of the tissue into definite anatomical structures.

Follicular collections of lymphoid tissue are found along the alimentary tract: (1) at the back of the mouth and nose, where there is a ring of lymphoid tissue consisting of the lingual, palatine, and pharyngeal tonsils; (2) in the lower part of the small intestine, as Peyer's patches; (3) in the cecum, as the vermiform appendix; and (4) in the large intestine as solitary follicles. Solitary follicles are also found scattered throughout the mucous and submucous layers of the small intestines, but they are most numerous in the lower part of the ileum. Aggregated collections of follicular lymphadenoid tissue are especially notable in the fauces and in the lower extent of the small intestine (ileum).

At the fauces the tonsils form parts of a band of lymphadenoid tissue which surrounds the opening into the esophagus and trachea. The anterior part of the ring is formed by the lingual tonsil on the posterior part of the tongue; the lateral portions consist of the palatine tonsils and the lymphadenoid tissue around the auditory tubes; posteriorly, the pharyngeal tonsil is situated on the posterior wall of the pharynx. In the intervals between these main masses smaller collections of lymphadenoid tissue are present.

In the small intestine the aggregated lymphadenoid collections are usually known as Peyer's patches and correspond, very markedly both

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anatomically and physiologically, with the faucial tonsils. Peyer's patches are largest and most numerous in the ileum; in the jejunum they are few in number, and occasionally they are seen in the duodenum. They are situated in the antimesenteric part of the intestinal wall. They are most marked in young individuals, become indistinct in middle life, and sometimes disappear altogether in advanced life. They are freely supplied with blood vessels which form an abundant plexus around each follicle and give off fine branches permeating the lymphoid tissue in the interior of the follicle. This is best demonstrated under the magnifying glass and under powerful transmitted light. Lymphatic plexuses are especially abundant around these patches and empty into the mesenteric lymph nodes.

Nonspecific granulomatous lesions are commonly present in the small intestine, usually in the distal portion; in the cecum and at the ileocecal junction; and they follow fairly closely the distribution of the aggregated collections of lymphadenoid tissue. In the aforementioned collected series, this represents approximately 58 to 59 per cent of the total number of cases. In the remaining cases, the incidence of the cases follows comparatively closely the distribution of lymphadenoid tissue elsewhere in the alimentary canal especially of the solitary follicles. This seems to be a very remarkable fact.

The available knowledge regarding pathologic lesions of the intestinal lymphadenoid tissue, including the solitary and aggregated follicles, indicates an astonishingly large incidence and includes typhoid fever, various forms of bacteriemia, status lymphaticus, tuberculosis, the various blood dyscrasias, a case of agranulocytosis reported by Felsen,[51] and the various forms of colitis and dysentery. The development of the lesions in typhoid fever is of great interest, especially with respect to the lesions in the various forms of colitis and dysentery and with respect to the lesions in mesenteric adenitis.

In *typhoid fever* the swelling and subsequent ulcerations in Peyer's patches and the secondary inflammatory reaction, etc., in the mesenteric glands and in the spleen are well known. Opinion differs as to whether the lesion is a surface infection with organisms that are swallowed, or whether the organisms enter the blood stream higher up and involve the Peyer's patches by the hematogenous route. In any event, however, the course of progression of the lesion from Peyer's patch to the mesenteric gland, etc., seems established.

The lesions in the lymphadenoid follicles in the various forms of *colitis and bacillary dysentery* have been amply alluded to in the previous parts of this communication.

2. *The Relationship of Nonspecific Granulomatous Lesions of the Alimentary Tract to the Abdominal Lymph Nodes (Mesenteric Adenitis).*— The lesions in the associated lymph nodes draining the various anatomic areas are also of interest in this discussion.

The lymphatic vessels draining the ileum, appendix, and cecum are especially numerous. Those draining the appendix and cecum are almost as numerous as the ileal group, since the lymphadenoid tissue in the appendix and cecum is abundant. They drain into the ileocolic group of glands which surround the ileocolic artery. Usually a single gland is situated between the layers of the mesenteriolum of the appendix.

The mesenteric lymph glands situated between the layers of the mesentery, are, according to Gray,[72] Deaver,[43] and other anatomists, considerably more than 100 in number and arranged in a number of groups; one lying close to the wall of the small intestine among the terminal twigs of the superior mesenteric artery; a second, in relation to the loops and primary branches of the vessels; and a third, along the trunk of the artery.

The mesocolic glands lie between the layers of the transverse mesocolon, in relation to the transverse colon, especially with the right and left colic flexures, and are occasionally found along the trunk of the right and middle colic arteries.

The superior mesenteric glands receive afferents from the jejunum, ileum, cecum, vermiform process, and the ascending and transverse parts of the colon; their efferents pass to the preaortic glands.

The inferior mesenteric glands are distributed along the course of the large intestine distal to the splenic flexure extending all the way to the rectum. The glands drain these portions of the alimentary canal.

According to the experimental observations of Thompson, the lymphoid tissue of the alimentary tract of the rabbit is normally associated with the presence of gram-positive bacteria. A deficiency of vitamin A causes (1) the numbers of organisms in the lymphoid tissue to be markedly increased, especially in the lymphoid tissue of the vermiform appendix; and (2) a progressive atrophy, so that in the later stages when signs of xerophthalmia begin to develop, the lymphoid follicles were represented by only a thin layer of leucocytes. Readministration of vitamin A caused a regeneration of the lymphoid follicles. This work requires confirmation, but it is suggestive of a reason for the decline in the protective mechanism of the organism against infection and also for the loss of immunity against bacterial infection in vitamin A deficiency.

My experience with mesenteric adenitis has been described on several previous occasions. The experience may be classified as follows:

A. *Acute Intra-Abdominal Lymphadenitis:* Cases occur in which the clinical picture resembles very markedly that of an acute attack of appendicitis and in which the pathologic anatomic findings consist of moderately enlarged glands which, microscopically, show a simple hyperplasia. No gross changes are demonstrably visible in the appendix or in the neighboring coils of small or large intestine, and the entire process subsides in the operatively proved cases spontaneously.

B. *Acute Suppurative Intra-Abdominal Lymphadenitis:* A small number of cases in which the glands are larger and go on to suppuration. Drainage of the resultant abscess is necessary. I am sure that some of the cases in this group go down in the records as cases of appendical abscess in which the appendix is thought to have sloughed out.

C. *Chronic Granulomatous Form of Mesenteric Adenitis:* Cases in which an excessive production of inflammatory or granulomatous tissue is produced, gluing together glands and adjacent loops of intestine. When exposed on the operating table, the resultant mass of tissue is large; the essential parts of the mass are not determinable; usually no help is available from bacteriologic or other laboratory methods; and the condition seems most obscure. In the postoperative period fever continues for indefinite periods; accumulations of pus break through and discharge from the abdominal wound; fecal fistulas form frequently; soon the patient becomes very anemic and transfusions of blood are necessary repeatedly; and in the unfavorable cases death occurs from the debilitating effects of the long, drawn-out illness.

In the present state of knowledge it must be assumed that all forms of adenitis of this type are secondary to a primary lesion in the territory drained by the given group of nodes. Inasmuch as the nodes in the ileocecal angle are related to the terminal ileum, the appendix, and the ascending colon, one must necessarily look for the primary lesion there. Knowledge of any kind concerning the latter is entirely wanting. It is, however, distinctly suggestive that in this part of the intestinal tract the lymphadenoid follicles are especially abundant and find their best development in Peyer's patches. The suggested connection is strongly supported by the well-known course of events in typhoid fever; i.e., ulceration of the Peyer's patches, mesenteric adenitis, etc. And the chain of events is further corroborated by similar phenomena which occur elsewhere in the body.

The situation is complicated by the fact that in many of the nonspecific granulomatous lesions described in the literature extensive degrees of adenitis and periadenitis are described, and in these the wall of the bowel also becomes involved so that the whole area is fused together into one solid mass. When, in a bad case, the tissues are all glued together by inflammatory exudate and thickening, it is difficult to unravel the course of development of the total lesion. The anatomic and microscopic picture is not always conclusive. Again one must return to bacteriologic and agglutination tests if one wishes to make a decision; but, as has been indicated before, this is not always as helpful as one could wish.

One must recognize, therefore, that either of these two courses of development may occur; that the differentiation is difficult and in some cases, at least, impossible.

A COMPARISON OF NONSPECIFIC GRANULOMAS OF THE INTESTINAL TRACT WITH OTHER SOMEWHAT SIMILAR HYPERPLASTIC INFLAMMATORY MASSES

1. *Inflammatory Swellings in the Neck Resulting From Cervical Adenitis.*—A group of inflammatory swellings in the neck situated in and about the cervical lymph glands becomes of interest at this point of our discussion. It is well known that the point of origin for cervical lymphadenitis may be (a) undemonstrable, (b) demonstrable in or about the teeth, or (c) demonstrable in the pharyngeal lymphadenoid tissue and tonsils. In any case the neck lesion may be as follows:

A. The lesion is limited to the glands with little or no periadenitis. This represents the counterpart to simple inflammatory mesenteric lymphadenitis.

B. Adenitis which goes on to suppuration.

C. The gland lesion is surrounded by extensive amounts of inflammatory exudate which oftentimes spreads into neighboring tissues and attains very large dimensions.

The similarity between the anatomic structures involved, pharyngeal and intestinal lymphadenoid tissue, tonsils and Peyer's patches; the fact that both of the areas are parts of the alimentary tract; cervical and mesenteric lymph glands; and the nature of the resultant lesions both in the neck and in the abdomen is most obvious.

In the neck, most marked examples of this type of hyperplastic, inflammatory, granulomatous swellings are the *woody ("holz phlegmone") phlegmons of the neck.* These are extensive areas of solid indurated granulomatous swellings, involving glands and periglandular tissues, often extending down to and below the clavicle and spreading onto the chest wall. They are accompanied by fever, prostration, and deterioration of the heart and circulation; usually they do not break down into large abscesses, although microscopic abscesses are distributed throughout the indurated tissue and may result fatally. These lesions have no evidences of syphilitic infection. They remind one very much of the extensive degrees of inflammatory granulomatous exudate which one sees in the belly in association with gland and intestinal conditions.

2. *Inflammatory bone lesions* frequently are surrounded by excessive amounts of granulomatous tissue. This becomes especially marked about the lower jaw. The new tissue is usually situated between the periosteum and the bone and in the periosteum itself.

3. *Foreign Body Granulomas.*—In the abdomen masses of hyperplastic inflammatory granulomatous tissue may surround the path of a foreign body in its attempted or completed passage from an intra-abdominal viscus to the skin. Sometimes the foreign body is not discovered.

4. *Inflammatory Masses in the Abdominal Wall Simulating Desmoid Tumors.*—Large inflammatory masses are found from time to time situated in and behind the tissues of the abdominal wall. They simulate

desmoid tumors. I remember several instances of this kind. The microscopic picture did not yield any information and the Wassermann reaction was negative. While some of these may be associated with a foreign body, others furnish no adequate information regarding their etiology. Schloffer[140] has described somewhat similar cases which occurred after herniotomy operations.

5. *Inflammatory Masses in the Omentum.*—Similar inflammatory masses are found in the omentum and have been described by Braun.[22] As a general rule, no etiologic cause can be discovered except occasionally when they are found associated with the irritation accompanying the constant passage to and from a hernial sac.

Inflammatory adhesions, thickenings of the omentum, such as are found in the neighborhood of infections or when constricted in a hernial sac, extensive fibrosis about the site of an ulcer, and these larger masses of inflammatory hyperplasias are all of similar causation and developmental process. They differ in the degree of momentum and period of activity, in the relative piling up of granulation or reparative tissue as compared to the destructive process, and continue as long as the infective or necrotic process remains unconquered. Thus, if no complication occurs, such as an obstruction of the bowels, the granuloma may grow to an easily palpable size, may include adjacent tissues in its mass, and may possess areas of softening or ulceration in contradistinction to other areas of indurated firmness. Indeed, the clinical picture resembles that of a malignant tumor. Neighboring glands are frequently enlarged, thus adding to the deception.

The inflammatory hyperplastic masses correspond to the infective granulomas first described in this country by Senn.[141] He described a granulomatous tumor, the result of a necrosis of tissue, usually due to some mechanical constriction of blood supply to the involved tissue, followed by a low grade infection, and followed finally by a reparative process. The necrosis, low-grade infection, and reparative process go hand-in-hand, but the reparative process predominates, resulting in a piling up of granulation tissue until a tumorlike mass is formed. In other words, we have a breaking down and a building up with the latter conquering.

6. *Pelvic exudates* as a post-partum complication or accompanying inflammatory pelvic disease are well known as well as the large extent to which they can grow. The origin of the infection is in the uterus or tubes; the tubes are thickened, rigid, and the ends are closed; the granulomatous tissue spreads out from the latter into the pelvic retroperitoneal space and often extends considerably above the pelvic brim. Adhesions of neighboring, secondarily infiltrated coils of rectum, sigmoid, or small intestine add to the total mass. The mass of granulomatous tissue spreads by lymphatic extension. When spontaneous healing occurs, all of this excess granulomatous tissue completely disappears so that hardly

a vestige of it remains. Nevertheless, recrudescences of the process and the exudate formation occur commonly with reproduction of the entire pathology, until the gynecologic organ or organs which initiate the lesion are removed.

One knows that many of these are due to gonorrheal infection. In the others the ordinary forms of bacteria are found. Anatomically there are some similarities between the pelvic exudate and the intra- and extramural exudate which characterizes intestinal nonspecific granulomatous lesions.

7. *Inflammatory Lesions Following Vascular Disturbances in the Wall of the Bowel.*—A typical example of this is the tubular stenosis which occasionally follows the reduction of a strangulated loop of bowel from a hernial sac. The lesion, however, has none of the characteristics of a nonspecific or other granulomatous lesion and is a pure fibrous atrophy resulting in a stenosis involving the entire length of bowel in which the circulation was compromised.

8. *Simple Penetrating Ulcer of the Intestine.*—The extraordinary amount of thickening which sometimes surrounds the site of a walled-off, simple penetration or perforation is essentially a peritoneal phenomenon and shows none of the characteristics of an intestinal lesion. The perforation itself is usually an embolic lesion.

9. *Radiation Lesions.**—Granulomatous lesions accompanied by extraordinary intensity of pain, scarring, fibrosis, and ulceration occur also after radiation therapy. The most common and best example is the form of proctitis which follows radiation therapy with radium for carcinoma of the cervix uteri. This form of granuloma, of course, has nothing in common with the form of granulomatous lesion which is the subject of this discussion.

10. *Intestinal Sarcoidosis.*—According to Longcope,[100] lesions resembling Corr and Boeck's[35] sarcoidosis have been described as occurring in the intestinal tract, particularly in the lower ileum and in the cecum, and some relationship has been suggested between this lesion and nonspecific granuloma. The pathologic lesions of sarcoidosis are most characteristic, however, and consist essentially of an epithelioid miliary tubercle which does not resemble in any way the microscopic picture of nonspecific granuloma. Whatever superficial resemblances occur result from the complete fibrosis which replaces the tubercle-like formations in the process of healing.

DISCUSSION

In discussing the etiology of nonspecific granuloma of the gastrointestinal tract, the following possibilities are present:

1. *That it is due to some vitamin deficiency.*

*The various forms of neoplasia obviously are not in any way associated with the subject under discussion.

2. *That it is due to some neurotrophic disturbance.*—At the present writing, knowledge regarding disturbances of the vitamin content of the body is still being developed. Certainly we have no knowledge regarding any possible relationship between any such disturbance and any form of granulomatous lesion of the intestinal tract. In looking for any possible connection, it is conceivable that the initial stages of any anatomic change (spasm, hyperemia, relative anemia, etc.), functional change (anoxemia or other obtuse chemical changes), or symptomatic manifestations (diarrhea, hemorrhage, pain, etc.) might be due to disturbances in the quantity or quality of a single vitamin or group of vitamins available in the body. Nevertheless, it is difficult to believe that the late stages associated with intramural infection, abscess, fibrosis, etc., could result from this disturbance alone without the addition of other factors.

Whatever knowledge we have available at the present writing indicates a fairly close relationship between disturbances of vitamin content and neurotrophic change (hitherto obscure forms of neuritis, such as, for instance, beriberi, pellagra, etc.). So that whatever relationship there might be between any neurotrophic disturbance and a granulomatous alimentary tract lesion probably would take place by way of some vitamin disturbance and would probably be initiated by the latter. At the present state of our knowledge, both vitamin disturbance and neurotrophic changes must be considered together.

3. *That it is primarily or essentially an allergic manifestation.*—Sensitization of various body areas or organs to chemical, bacterial, or other toxins occurs as a primary manifestation or as a secondary phenomenon following definite forms of infection or toxemia. There is considerable ground for believing, especially from the way the symptomatology of the various forms of colitis (using the latter term in its broadest sense) behave, that the relatively sudden intensifications, exacerbations, and recrudescences of symptoms might be based upon an allergic mechanism and might be associated with the sensitization of the alimentary tract to the primary cause of the disease.

Taking the three preceding factors together, it is not an easy matter to formulate accurately the relationship of any one of these to each other, or to the disease under discussion. Nevertheless, while it seems that many times one or all of these factors play a part in enhancing the anatomic changes or clinical manifestations, it is difficult to believe that any of them are the direct inciting cause of nonspecific granuloma of the alimentary tract.

4. *That it is caused by secondary invasion of the wall of the alimentary canal from an extrinsic lesion (lymph nodes).*—Upham[157] has suggested that an infection occurs in the ileocecal area which has but slight local effect on the mucous membrane, but a marked secondary effect on the glands in the drained area; an ileocecal lymphadenitis becomes estab-

lished. Combining this with the work of Reichert and Mathes[131] that irritating and sclerosing materials injected into the mesenteric and subserous lymphatic vessels produce sclerosis and thrombosis of the lymphatics, leading to a chronic lymphedema, Upham arrives at the conclusion, based upon these two hypotheses, regarding the origin of regional enteritis: that degenerative processes in the ileum or whatever portion of the intestine may be involved, follow, and that regional enteritis is the endstage, the primary stage being mesenteric lymphadenitis from upper respiratory tract infection (Pribram's hypothesis).

It seems to me that the opinion expressed by Upham,[157] Pribram, etc., that the same etiologic factor which causes the enlarged lymph nodes also causes the intestinal lesions simultaneously, which, so to speak, puts the cart before the horse, has in no way been proved and seems to me to be inaccurate. The more correct viewpoint in my opinion is that the intestinal lesion comes first; that the lymph nodes are secondary thereto; and that the latter have no separate etiologic basis. I think that the error has been made in the last group of mesenteric adenitis cases described in which excessive amounts of inflammatory exudate form and in which it is more than easy for confusion to occur in the interpretation of the demonstrable anatomic picture.

5. *That it is due to some specific infection such as infection by the Bargen*[10] *organisms, by an organism of the dysentery group, etc.*—At the Mayo Clinic, Bargen's[10] organism is found in 90 per cent of the cases; the finding is corroborated by animal reproduction of the disease; and a vaccine, a culture filtrate, and a therapeutic horse serum have been developed which are said to be helpful. The work has not been accepted in many quarters and Brown[24] and Paulson,[117] of the Johns Hopkins Hospital, have been particularly outspoken in their criticism, basing their conclusions on the following items: (a) that only one-third of the cases were studied; (b) that they do not approve of the agglutination methods; (c) that Bargen's work was not properly controlled; and (d) that the bacteriologic characteristics of the organism were not constant. In addition, Paulson was able to reproduce similar lesions in rabbits with organisms normally present in healthy individuals. It seems, therefore, that the best one can say for Bargen's[10] organism is that the work needs considerable corroboration before it can be accepted. The opinion in many circles is that Bargen's organism is a secondary invader.

Infection by organisms of the dysentery group has assumed and continues to assume a dominating position. The entire subject seems intimately bound up with the various forms of colitis.

Felsen's[51] contention that nonspecific granulomatous lesions of the intestinal wall are primarily infections by organisms of the dysentery group is a further exposition of Hurst's[79] suggestion, in which the late stage of the dysentery infection becomes a nonspecific granuloma, has found only slight corroboration in the carefully restricted and guarded

statement of Winkelstein.[164] There is no other corroboration available at the present time. A personal communication from Bargen, of the Mayo Clinic, tells me that there this question was thoroughly investigated and for want of evidence discarded.

Most of Felsen's evidence is based upon bacteriologic agglutination and bacteriophage studies. According to Winkelstein,[164] who presents a somewhat opposing viewpoint:

"The identification of the organisms requires great care. The cultural characteristics alone are insufficient. In fact, using the cultural characteristics alone for diagnosis, one would be forced almost each day to report atypical *B. coli* obtained from various sources (gall bladder, genito-urinary tract, normal stools) as dysentery organisms. The agglutination in high titre of the organism by specific sera is absolutely essential for the diagnosis of an organism as a bacillary dysentery strain. . . .

"Agglutinins for dysentery organisms, while usually not of a very high titre, may occur in the blood of normal people.

"The mere finding of agglutinins in the blood is not diagnostic of bacillary dysentery. Gross agglutinins from closely related bacteria (*B. coli*) may also confuse the situation. Agglutinins may appear and disappear rapidly, or, may appear late, or, may not appear."

As far as the bacteriophage goes, Winkelstein points out that a weak bacteriophage for *B. coli* is commonly present; and if, for various reasons which he points out, it should become strongly lytic, a similar effect can be obtained upon closely related stock organisms of the dysentery group. So that the mere finding of a dysentery bacteriophage does not necessarily prove the dysentery bacillus origin of the infection. However, at the Mt. Sinai Hospital, "the finding of a dysentery bacteriophage in a fairly high percentage of the cases of ulcerative colitis of undetermined etiology and not in normal and miscellaneous controls, is assumed to be somewhat suggestive of the dysentery origin of the disease but for the reasons just cited, not conclusive evidence."

There is no sharp line of differentiation or demarcation clinically between the late stage colitis and the granuloma groups. Anatomically, the pathologic changes can present very similar pictures. Frequently there is great difficulty in obtaining adequate and/or reliable bacteriologic data upon which an opinion regarding the etiology of the given lesion can be based. Everyone of experience has seen the transition from one to the other type of lesion in the same case and, according to Winkelstein, this is particularly true of the group of lesions in the terminal ileum.

6. *That it is due to some combination of factors indicated in the preceding items.*

7. *That it is the end or terminal stage of some preceding lesion and that it is due to a secondary invader, or to a mixed infection with organisms which have not yet been identified; or,*

8. *That it is the end result of more than one preceding intrinsic lesion and is caused, with or without the aid of some of the other factors mentioned by the transfer of a surface (mucous membrane) lesion, to the deep layers of the wall of the alimentary canal.*

SUMMARY AND CONCLUSIONS

The available facts reviewed in this communication indicate that hypertrophic granulomatous lesions are encountered in infections with amoebae, in infections by various strains of the dysentery group, in the group of so-called nonspecific ulcerative colitis, associated with previously existing conditions, such as diverticulitis, or as a chronic development unassociated apparently with any preceding condition. Similar lesions are found in the post-partum period or associated with inflammatory disease of the adnexa. In addition, somewhat similar lesions are found in the neck and under other conditions in the abdominal cavity unassociated with the intestinal tract, so that it seems that the granulomatous lesion is rather widespread in the body and of a diverse protein character. In any case, in the gastrointestinal tract the characteristic part of the lesion consists in a spread of a surface lesion to an intramural position in the wall of the alimentary canal. Essentially the lesion seems to be a form of chronic infection of the lymphatic apparatus of the deeper layers of the bowel wall which implicates the solitary and aggregated collections of lymphadenoid follicles, the lymphatic channels, and the associated lymph nodes in the appropriate part of the mesentery. During the development of the lesion, the original agent of infection commonly disappears and secondary infection takes place. As a consequence of this, intramural abscesses form. During the healing or attempted healing of the latter, cicatrization is accompanied by the excessive production of scar tissue; and the latter causes a hypertrophic thickening of the bowel wall with subsequent stenoses.

In view of the several different original etiologic factors or conditions, it seems difficult to ascribe this lesion to any one original cause. My own opinion inclines me to the belief that the nonspecific granulomatous lesion is a nonspecific one, not only because some original specific factor has disappeared, but because the granulomatous lesion may follow more than one somewhat similar or distinctive agents or conditions; and that the granulomatous part of the lesion represents an end result of a diversely initiated lesion of bowel infection marked by final or secondary intramural infection and subsequent evidences of an attempted overproductive but unsuccessful healing.

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Review of Recent Meetings

REVIEW OF SECTION ON GENERAL AND ABDOMINAL SURGERY, AMERICAN MEDICAL ASSOCIATION, MAY 17 TO 19, 1939, ST. LOUIS, MO.

MICHAEL DEBAKEY, M.D., NEW ORLEANS, LA.

FRED COLLER, Henry K. Ransom, and Charles Sherrill Rife, Ann Arbor, Mich.: **Further Experimental Studies on Reaction of the Peritoneum to Trauma and Infection.**—The authors performed various abdominal operative procedures, such as gastroenterostomy, enterocolostomy, colostomy, and "precolostomy," on the dog in an attempt to determine experimentally whether the peritoneum can be protected against infection. *Bacillus coli* organisms were used as the infective agent and the minimum lethal dose by intraperitoneal injection was found to be "one-fourth slant." Whereas the survival time of the animals was used as one criterion for determining the degree of immunity conferred on the peritoneum by the various operative procedures, the cellular response of the peritoneum, i.e., the mobilization of polymorphonuclear leucocytes and the amount of phagocytosis, was considered a better quantitative method. The results of inoculation two weeks after an operative procedure such as colostomy showed a marked increase in the total leucocyte count of the peritoneal fluid but considerably less if the inoculation was done four weeks after the operative procedure. The authors concluded from their studies that not enough immunity was conferred on the peritoneum by such operative procedures to justify stage operations.

Bernhard Steinberg, Toledo, Ohio: **Stages in Peritonitis Based on the Defense Mechanism in Relation to Treatment.**—Peritonitis is a progressive condition characterized by three stages: (1) the primary stage, in which the defense mechanism is maximal; (2) the secondary stage, in which the inhibitory elements become manifest; and (3) the tertiary stage, in which irreparable damage to tissue occurs. From the prognostic as well as the therapeutic standpoint, it is important to determine the stage of the condition. In the primary stage the body defense mechanism can be enhanced by the use of bactrogen. In the secondary stage this procedure is of no value. Attempts should be made to conserve the cardiovascular system. Small transfusions (200 c.c.) are helpful. In the tertiary stage there is little that can be accomplished. The respective stages can be determined by examining microscopically a smear of the peritoneal fluid obtained at operation or by a specially devised aspirating needle. Numerous leucocytes and only three bacteria or less in a high-powered field characterize the first stage. Fewer leucocytes and four to six bacteria suggest the second stage. Leucocytes in process of disintegration and ten or more bacteria indicate the tertiary stage.

George D. Lilly, Miami, Fla.: **Complications of Appendical Peritonitis.**—Emphasis was placed upon the necessity of distinguishing between appendicitis and appendical peritonitis. In the former the inflammatory process is limited to the appendix and immediate surgical intervention is indicated. On the other hand, in the latter the inflammatory process has extended beyond the walls of the

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appendix and peritonitis either localized or generalized becomes the important consideration. Once peritonitis has developed, conservative management is indicated because of the characteristic tendency of the peritoneum and omentum to localize the process with adhesions. Surgical intervention during this stage is undesirable because the manipulations of the surgeon result in the breaking down of these protective adhesions and the consequent dissemination of the infection.

The most common complications of appendical peritonitis are virulent infection, residual abscesses, and pylephlebitis. A succinct discussion of the incidence, clinical manifestations, diagnostic criteria, and proper management of each of these complications was then presented. Emphasis was placed upon the Nather-Ochsner extraserous approach in the drainage of subphrenic abscess.

These three presentations were discussed together: **Claude F. Dixon,** Rochester, Minn., stated that he is convinced of the value of intraperitoneal vaccination, especially in surgery of the colon. He cited a series of 180 such operative cases in which intraperitoneal vaccination was performed with a total mortality of 6 per cent, as compared with a similar series in which vaccination was not done with a total mortality of 17 per cent. In studying the cellular response to intraperitoneal vaccination, he found that the peritoneal fluid count rose from 2,000 to 96,000.

Fred Coller, Ann Arbor, Mich., stated that peritoneal immunity is due to a hyperproduction of leucocytes and that the prognosis can be determined by studying the bacterial and cell counts on a smear of one drop of the peritoneal fluid. Whereas the local peritoneal reaction is important in the prognosis, of equal significance is the general condition of the patient. Every attempt should be made to combat distention, dehydration, and anoxia by appropriate therapeutic measures, and operative manipulation in the peritoneal cavity should be reduced to a minimum. Coli bactrogen should not be employed routinely in abdominal operations but is indicated in cases in which gross contamination has occurred.

J. Shelton Horsley, Richmond, Va., stated that he treats all cases of appendicitis, regardless of the stage of the process, by immediate operation. The McBurney incision is employed routinely. The operative removal of the appendix consists of ligation, severance with the cautery, and cauterization of the stump with pure phenol. In a series of 885 cases of appendicitis treated in this manner, there were 5 deaths.

W. Wayne Babcock, Philadelphia, Pa., stated that there are four important factors in the consideration of peritonitis: (1) toxic, (2) propagative, (3) diffusing, and (4) protective factors. He discussed the principle of "internal exteriorization" in the treatment of appendical abscess and presented slides illustrating the use of glass "lamp chimney drains" to which is applied constant suction.

Alton Ochsner, New Orleans, La., emphasized the necessity of differentiating appendicitis and appendical peritonitis because of the difference in prognosis and treatment. One of the most frequent and most serious complications of appendicitis is subphrenic abscess. This is shown by the fact that in a series of 3,533 collected cases of subphrenic abscess recently analyzed by Dr. Ochsner and **Michael DeBakey,** New Orleans, La. (Internat. Abst. Surg. 66: 426, 1938), the origin was from the appendix in 30.9 per cent. The gravity of this complication is illustrated by the fact that in a series of 3,038 collected cases the general mortality was 53.5 per cent. The site of localization of subphrenic abscess is of particular significance from the standpoint of treatment. In a series of 1,532 collected cases, the subphrenic abscess was localized on the right side in 906 (59 per cent), on the left side in 493 (27.6 per cent), on both sides in 68 (4.4 per cent), and retroperitoneally in 223 (14.5 per cent). Emphasis was placed upon the method of drainage of these abscesses. Thus, of 394 collected cases drained

transpleurally and 327 cases drained transperitoneally, the mortality rates were 36.2 per cent and 35.1 per cent respectively; whereas, of 211 cases having extraserous drainage, the mortality was 20.8 per cent.

Walter M. Boothby, Charles W. Mayo, and W. Randolph Lovelace, II, Rochester, Minn.: **One Hundred Per Cent Oxygen: Indications for Its Use and Methods of Its Administration to Surgical Patients.**—A brief review of the indications and value of oxygen therapy was presented. Whereas the various methods previously described for the administration of oxygen in the inspired air permitted only 50 to 60 per cent concentration, the present method utilizing a specially devised mask allows 100 per cent concentration, according to the authors. It presumably has the advantages of simplicity, efficiency, and economy. The authors stated that it is of special value in shock, coronary thrombosis, pulmonary embolism, gas gangrene, intestinal distention, and for the relief of headache which follows encephalography.

Alvan L. Barach, New York, N. Y., in the discussion, stressed the value of 100 per cent oxygen therapy in peripheral circulatory collapse, pneumonia, coronary occlusion, and asthma. However, it should not be administered continuously longer than two days because of the irritation to the endothelium.

Jacob Fine, Boston, Mass., stated that the inhalation of 100 per cent oxygen from one-half to three hours usually relieves headaches which follow encephalographic procedures. He emphasized its value in distention and explained its rationale on the basis of greater elimination of nitrogen.

Loyal Davis, and John Martin, Chicago, Ill.: **Surgical Lesions in the Paratrigeminal Area.**—In the paratrigeminal area there is situated the gasserian ganglion and its divisions, the internal carotid artery, sympathetic nerve fibers, and the three cranial nerves which innervate the extraocular muscles. Pressure upon these structures by lesions which may occur in this area produces a characteristic syndrome. There are two lesions which have been encountered: aneurysm of the internal carotid artery and meningiomas of the dural envelope which encloses the gasserian ganglion. Six cases of the latter type have been operated upon. The clinical manifestations usually observed are: constant pain and patchy areas of sensory loss in the face, dilated pupil, ptosis of the upper eyelid, and partial or complete paralysis of the extraocular muscles. The differential diagnosis was discussed briefly.

Ernest Sachs, St. Louis, Mo., stated that he operated upon the first case of this type in 1915 and reported it two years later. In differentiating this condition from tic douloureux, it should be recalled that pain in the former is constant and in the latter is intermittent. Moreover in this syndrome the motor root of the fifth nerve is involved, whereas in tic douloureux it is not.

Albert Behrend and Helena E. Riggs, Philadelphia, Pa.: **Cerebral Complications Following Surgical Operations.**—The authors emphasized the frequency of such postoperative cerebral complications as prolonged coma, convulsions, disturbances of psychic function, focal cerebral symptoms, and hyperpyrexia. Among several surgical services at the Philadelphia General Hospital, these complications were observed in twenty-one patients, an incidence of 6 per cent. They occur following any type of anesthesia and are seldom associated with cerebral thrombosis, embolism, or hemorrhage. Damage to brain cells as a result of anoxia due to cardiocirculatory insufficiency is believed to be the cause of these complications. Lantern slides showing microscopic sections of the brain tissue revealed the characteristic lesion to be a parenchymatous edema and chronic interstitial fibro-

sis. The authors explained the development of these complications on the basis of three factors which combine to produce a fall in blood pressure and consequent cerebral anoxia: (1) the anesthetic, (2) the operative procedure, and (3) a pre-existing cardiocirculatory dysfunction which may or may not be apparent. The prevention and treatment of these complications were discussed briefly.

Henry K. Beecher, Boston, Mass., in the discussion, agreed with the authors that cerebral anoxia is the likely cause of these complications. However, he disagreed with the concept that pre-existing vascular lesions were an important factor. He suggests that the investigations, especially as regard the microscopic studies, should be controlled better by routine autopsy material.

F. H. Lewy, Philadelphia, Pa., also discussed the presentation and directed attention to vasolability as a possible factor in the development of these complications.

Alton Ochsner and Michael DeBakey, New Orleans, La.: **Thrombophlebitis, the Role of Vasospasm in the Production of the Clinical Manifestations.**—The authors expressed the opinion that the concept that mechanical blockage of the venous and lymphatic systems is of primary significance in the production of the clinical manifestation in thrombophlebitis is inadequate. In the light of their clinical and experimental investigations, it is believed that many of the symptoms and signs are due to vasospasm in the arterial and venous systems and that the vasoconstrictor impulses originate in the thrombophlebitic segment. Numerous reported clinical observations have indicated that a localized thrombophlebitic process can initiate a marked vasospasm. The authors briefly described their clinical and experimental investigations which demonstrated the occurrence of vasospasm in the presence of thrombophlebitis. They were able to show that the vasoconstrictor impulses originate in the involved segment and are transmitted over the sympathetic nervous system. Because of the vasospasm, there result increased filtration pressure, relative anoxia of the capillary endothelium, and diminution in the flow of lymph, all of which increase the amount of perivascular fluid. Accordingly, by interrupting the vasoconstrictor impulses by procaine hydrochloride infiltration of the sympathetic ganglia, there is produced a re-establishment of the normal exchange of intravascular and perivascular fluids.

This method of therapy has been employed in fifteen cases with seventeen thrombophlebitic processes and the results presented. There was prompt and permanent relief of pain in all instances. In one-half the cases the temperature returned to normal within forty-eight hours and in the other one-half, within one week. In over one-half the cases the edema subsided in eight days and in the remaining cases, within twelve days. Sixty per cent of the cases were discharged from the hospital as cured within eight days after the institution of therapy.

In the discussion, **Géza de Takats,** Chicago, Ill., stated that the dramatic results obtained by the authors deserve wide attention. The concept that reflexes originate from the site of a vascular block has been demonstrated and its significance in the treatment of acute vascular occlusions realized. He referred to the investigations by himself and **George K. Fenn,** Chicago, Ill., which showed that vagal reflexes originate from the occluded pulmonary artery in pulmonary embolism and radiate to the heart, bronchi, and gastrointestinal tract. He cited personal observations confirming the authors' results. Thus, not infrequently the hard edema present in patients suffering from Buerger's disease and resistant to rest in bed may disappear promptly after sympathectomy. Sympathetic denervation readily relieves the hard traumatic edema of Sudeck's atrophy. Whereas sympathetic block produces greater vasodilatation, in the milder cases of throm-

bophlebitis papaverine in ½ gr. doses may be of value. Reference was made to the fact that early mobilization of patients did not result in an increased percentage of embolization. With **J. H. Jesser,** Chicago, Ill., Dr. de Takats recently analyzed 100 cases of massive pulmonary embolism and found only 11 with manifestations of thrombophlebitis. In 9 of these the manifestations appeared after the pulmonary embolism. Emphasis was placed upon the fact that patients react with different intensity to an identical vascular accident. Whereas in some patients there may be complete disappearence of arterial pulses simulating arterial occlusion, in others vasodilatation occurs. However, this premonitory vasodilatation may give rise to a marked vasoconstriction as the thrombus becomes larger.

John R. Paine, Minneapolis, Minn., stated that he and **C. J. Bellis,** Minneapolis, Minn., have been studying cases of thrombophlebitis with respect to the tissue tension, the skin temperature, the venous pressure, and the venogram. The tissue tensions usually have been within normal limits, as have the skin temperatures. The venous pressure usually has been slightly elevated. The venograms are difficult of interpretation, but frequently they show definite scattered areas of spasm in the demarcated veins. Since the fall of 1938, they have treated 7 cases of acute thrombophlebitis of the deep veins of the legs and 13 chronic cases by means of intermittent venous occlusion. The cuffs have been applied to the thighs and a pressure of 70 to 80 mm. Hg. with a four-minute cycle used. Treatment for three to four hours a day has been continued for a variable period. In only 2 cases, both of an acute nature, have pain and discomfort not been relieved. In about one-half of the cases edema has been decreased. The results obtained have been due in part, they believe, to release of vasospasm. The acute cases have been treated with considerable trepidation, but no embolic accidents have occurred. The effect of this type of treatment on the pulse and temperature of the acute cases has been noteworthy.

Sedgewick, Joneston, Ohio, stated that he has employed novocain block of the sympathetics in thrombophlebitis with excellent results. As a result of the presentation, he now understands the rationale.

Frederick W. Taylor, Indianapolis, Ind.: **Arteriosclerotic Gangrene: Relation of the Amputation Stump to Morbidity and Mortality.**—The high operative mortality in arteriosclerotic gangrene with or without diabetes was emphasized. Thus, in a series of 90 major amputations the case mortality was 37.6 per cent and the amputation mortality was 32 per cent. Whereas there are other significant factors, attention was directed particularly to the relation of operative procedure and stump healing to mortality. On the basis of the present series, the author found that the usual anatomical fascial plane closure in the majority of instances (a) devitalizes the already poorly nourished stump tissues, thus predisposing to necrosis and suppuration; (b) allows inadequate drainage for infected cases; (c) results in only a small number of promptly healing stumps, 19 of 90 amputations; and (d) definitely increases the operative risk and does not shorten the average postoperative hospital stay (49.5 days as compared with 51.5 for the no-suture secondary closure method and 37.5 days for the procedure of loose skin closure only). On the basis of this analysis, the author concluded that in the great majority of arteriosclerotic gangrene amputations no consideration should be given skin flaps or stump repair and that the simple circular amputation is by far the safest procedure. In those cases in which the danger of infection exists, no attempt should be made to close the stump. If infection is but a slight hazard, the skin may be closed with a few interrupted sutures. In the extremely septic patient, often with an uncontrollable diabetes, the author rec-

ommended simple chop amputation at or just above the knee. The anatomical fascial plane suture of the stump should be reserved for the exceptional case with no infection and an abundant blood supply.

In the discussion, **Willis D. Gatch**, Indianapolis, Ind., stated that the no-suture guillotine type of amputation usually below the knee was the safest procedure in the presence of fulminating infection. A cod-liver oil dressing is applied to the open wound. The safest type of closed amputation is performed with a circular incision, usually in the supracondylar region. In a series of 100 cases with diabetes, the mortality was 14 per cent and healing by primary union occurred in 93 per cent.

Henry H. Faxon, Boston, Mass.: **Major Amputations in Advanced Peripheral Arterial Obliterative Disease.**—This report was based upon an analysis of 530 cases of peripheral arterial disease admitted to the Circulatory Clinic of the Massachusetts General Hospital from 1929 to 1939. Of this number, 112 were diagnosed as Buerger's disease; 176, as arteriosclerosis; and 242, as arteriosclerosis with diabetes. There were 262 cases requiring major amputations, of which 204 were single and 58 were bilateral. General considerations in the management of these conditions were presented. The guillotine amputations were performed only in the very sick patients (10 per cent). In this group the operative mortality was 25 per cent. None of the cases of Buerger's disease died; 25 per cent of the arteriosclerotic group and 32 per cent of the cases having arteriosclerosis with diabetes died. Of the 530 cases, 40 per cent had primary closed amputations with a mortality of 9.6 per cent.

In the discussion, **Géza de Takats**, Chicago, Ill., directed attention to the importance of determining the site of amputation and pointed out that the histamine wheal test is of value.

Henry W. Cave, New York, N. Y.: **Chairman's Address: Chronic Intractable Ulcerative Colitis; a Surgical Problem.**—Medical management and surgical procedures less radical than the complete removal of the diseased bowel in extensive, intractable chronic ulcerative colitis have proved inadequate. Emphasis was placed upon the preoperative care of the patients. Anemia, dehydration, and vitamin deficiencies must be combated. Accordingly, repeated small blood transfusions, the daily intravenous administration of 5 per cent glucose, and the institution of vitamin therapy are valuable. Daily colonic irrigations with warm saline solution are indicated, especially prior to the second-stage operation.

Those cases requiring total colectomy should have the procedure performed in several stages. Complete diversion of the fecal stream should be done at the first stage. Moreover, it is desirable to do this sufficiently early in the course of the disease. Appendicostomy, cecostomy, and colostomy are of little or no value. The operative technique employed by the author was described and illustrated by means of lantern slides. Permanent ileostomy approximately six inches from the ileocecal valve is performed through a right McBurney incision as the first stage in those cases requiring total colectomy. At the second stage, five to eight weeks or even longer after the first stage, the small segment of terminal ileum, the ascending, transverse, descending, and upper sigmoid colon are removed through a left paramedian incision. The third stage, from two to six months later, is performed as a combined abdominoperineal resection. Subtotal colectomy may be employed in a few selected cases with proved normal sigmoid and rectum, the first consisting of end-to-side ileosigmoidostotomy and the second of subtotal colectomy. This has been done in 11 cases with 1 death. In the total series of 158 cases of ulcerative colitis, 27 were operated upon with 5 (18.5 per cent) deaths.

John D. Stewart, Boston, Mass.: **Control of the Hemorrhagic Tendency in Obstructive Jaundice by the Use of Vitamin K.**—The author reported the results of an investigation of the plasma prothrombin content in patients with obstructive jaundice and biliary fistula. It was observed that the plasma prothrombin level in these cases was usually low and that following operation further reduction in the plasma prothrombin may occur. Plasma prothrombin concentration less than 50 per cent normal may result in dangerous bleeding. By administering a mixture of vitamin K and bile salts, the plasma prothrombin was restored to normal and the bleeding tendency controlled. The author believes that the plasma prothrombin level depends not only upon the absorption of vitamin K from the intestines but also upon the functional capacity of the liver.

In the discussion, **H. P. Smith,** Iowa City, Ia., stated that vitamin K should always be administered when the prothrombin level dropped below 70 per cent. He suggested that the prothrombin level may be a test of liver function. **Hugh R. Butt,** Rochester, Minn., stated that normal prothrombin level does not necessarily mean that the patient will not bleed postoperatively. **W. Frank,** Louisville, Ky., stated that he has observed the occurrence of hematemesis in patients when the prothrombin level reached 65 per cent.

Conrad J. Baumgartner, Los Angeles, Calif.: **Congenital Lesions of the Neck.**—Emphasis was placed upon the necessity of a fundamental knowledge of the embryology of the neck in a surgical consideration of congenital lesions in this area. By means of lantern slide demonstrations, the embryologic development of structures of the neck was briefly described. Thyroglossal cysts and fistulas, branchial cysts and fistulas, and cystic hygromas were considered the most important congenital lesions of the neck. Their embryologic development and clinical manifestations were described. The treatment of these lesions consists of radical excision. However, in cystic hygroma radium therapy may be employed also. The operative technique was described and illustrated.

In the discussion, **Herbert Willy Meyer,** New York, N. Y., called attention to the masterly contribution of Wenglowski, who, on the basis of a study of a large number of human embryos from 2 to 49 mm., propounded a sound explanation for the embryologic development of these congenital lesions.

Manuel Grodinsky, Omaha, Neb.: **Ludwig's Angina, Retropharyngeal Abscess, and Other Deep Abscesses of the Head and Neck.**—A description was given of the fasciae of the head and neck based upon a study of seventy-five adult cadavers and five full term fetuses. The method of study consisted of dissection, injection, and section. This description was illustrated by means of lantern slides. Emphasis was placed upon the necessity of a fundamental knowledge of the anatomy of these structures in the consideration of the surgical treatment of infections in this area. In Ludwig's angina infection may spread from the floor of the mouth to the submandibular space, the lateral pharyngeal space, the space between the visceral and alar fasciae, and the space between the alar and prevertebral fasciae. Stress was placed upon the significance of spread of infection from the space between the visceral and alar fasciae to the superior mediastinum, as well as from the space between the alar and prevertebral fasciae to the posterior mediastinum.

Fred A. Coller, Ann Arbor, Mich., and **Louis J. Birsner,** St. Louis, Mo., discussed the presentation.

Harvey B. Stone and **Samuel McLanahan,** Baltimore, Md.: **Surgical Aspects of Carcinoma of the Large Bowel.**—The authors stressed the fact that delay in diagnosis is still one of the most important problems in the consideration of

carcinoma of the large bowel. The early recognition of these lesions forms one of the most significant factors in operability, which in turn influences the mortality rate. Emphasis was placed upon the value of one-stage operative procedures for growths on both the right and left sides. They stated, however, that the two-stage procedures are probably better in the poor risk cases. Attention was directed to careful technique in aseptic end-to-end anastomosis. The abdominoperineal route was usually employed, most often in one stage, in operable rectal cancers. The authors presented their statistics on operability and mortality.

In the discussion, **James D. Rives,** New Orleans, La., stated that the success of any operative procedure on the large bowel, in his opinion, depended upon three factors: (1) careful preoperative preparations, (2) aseptic technique with no tension on the suture line to prevent possible leakage, and (3) careful handling of the gut to prevent injury to vessels and a resulting thrombosis.

Leland S. McKittrick, Boston, Mass., stressed that in his experience he had found two-stage operations for malignancy of the large bowel were preferable, particularly in poor risk cases. He expressed his admiration for the work of Dr. Stone and Dr. McLanahan, but he felt that in his hands mortality was much less with the two-stage procedure. He stated that success in operative procedures of this type depends upon four important factors: (1) adequate blood supply at the site of the anastomosis, (2) avoidance of tension on the suture line, (3) avoidance of pressure in the anastomosed gut, and (4) routine preliminary colostomy.

Henry Ransom, Ann Arbor, Mich., stated that at Ann Arbor, at the present time, the two-stage procedure is being used routinely. He expressed the opinion that, whereas the two-stage procedure gives only a slightly increased protection against peritonitis, in the poor risk cases, because of less trauma, it is much better than a single-stage operation.

Claude F. Dixon, Rochester, Minn., stated that he preferred the two-stage operative procedure and in his hands the mortality rate was lower. He advocated the routine administration of vitamin K in these cases as a preoperative measure to increase the coagulation time. He felt that this was indicated because of a certain number of deaths due to massive hemorrhage occurring a few days after operation at the site of the anastomosis.

Frank H. Lahey, Boston, Mass., stated that at the Lahey Clinic these procedures are always performed in two stages. The operability at the Lahey Clinic is 89.9 per cent and the mortality is about 10 per cent. He stressed the difference between contact carcinoma in the peritoneum and frank metastatic lesions and stated that frequently the surgeon fails to recognize the difference in these two conditions and consequently considers the case inoperable.

Harvey B. Stone, Boston, Mass., in closing the discussion, stressed three points: (1) the importance of aseptic technique; (2) the value of the one-stage operation which he believes has its field of usefulness, particularly in the good risk cases, but for which cases must be chosen, too much emphasis possibly having been placed on the one-stage procedure; and (3) the fact that evidence of an isolated polyp in the rectum which seems to be clinically benign may be malignant. He stated that he had nine cases of this type. He advocates the local removal with a very close postoperative follow-up, and, if there is evidence of a recurrence, radical resection of the rectum is indicated.

I. S. Ravdin, Alfred Stengel, Jr., and Cecilia Riegel, Philadelphia, Pa.: **Hypoproteinemia in Surgical Patients.**—The authors emphasized the fact that hypo-

proteinemia in patients with lesions of the upper gastrointestinal tract as well as with lesions of the biliary tract occurs more frequently than is commonly realized. As a result of hypoproteinemia, edema of sufficient degree may develop at the site of a new stoma to produce obstruction. Attention was also directed to the significance of hypoproteinemia in the failure of wound healing. The authors have overcome the hypoproteinemic states by the administration of amino-acid solutions, peptone hydrolysates, and normal and lyophile serums. The method employed was briefly described.

Robert Elman, St. Louis, Mo., in the discussion, emphasized the need of a well-balanced diet in handling gastrointestinal cases. He drew attention to the fact that often the diet administered to this type of patient is deficient in proteins.

Harold Lincoln Thompson, Los Angeles, Calif.: **The Immediate and Late Results of Surgical Treatment of Acute Perforation of Peptic Ulcer.**—Five hundred cases collected in a ten-year period from Los Angeles County were reviewed. These cases were from all of the hospitals in that location. The general mortality rate was 26.5 per cent. He stressed the fact that the mortality rate was higher than it should have been due to a number of factors not under the control of the surgeon, particularly the delay of the patient in seeking treatment. He presented one group of cases in which expectant treatment was used and in which the mortality rate was rather low for this form of therapy. Spinal anesthesia was found to be preferable to general anesthesia by a small margin in this series. Simple closure was the procedure of choice in operation.

In the discussion, **Dan C. Donald**, Birmingham, Ala., presented a series of cases from that city. His mortality rates were much the same as those of Dr. Thompson. He agreed with Dr. Thompson regarding the operative procedure as well as the anesthetic of choice.

J. W. Thompson, St. Louis, Mo., presented a series of cases from the City Hospital in St. Louis in which the general mortality in ruptured ulcer was 25.7 per cent.

C. B. Odom, New Orleans, La., presented a series of lantern slides prepared from a review recently made by **Michael DeBakey**, New Orleans, La., and himself of 211 cases admitted to Charity Hospital between the years of 1929 and 1939.

It was shown that, whereas according to this survey over a ten-year period the incidence of gastroduodenal ulceration in general has increased approximately one and one-half times, acute perforations have increased about seven times. Contrary to a prevalent belief, the incidence in the white and colored races in this series was almost equal. As has been repeatedly demonstrated, there was a preponderance of the male sex (98.1 per cent). The operation of choice is simple closure. Whereas of 200 cases in which simple closure was used, only 33 (16.5 per cent) died; of 7 cases in which the more radical procedures were employed, 3 (42.8 per cent) died. The type of anesthetic was also found to be significant in the prognosis. Thus, of 7 cases in which epidural block and of 154 cases in which spinal anesthesia were used, the mortality incidences were 0 per cent and 15.7 per cent, respectively; of 43 cases in which general anesthesia and of 5 cases in which local analgesia were employed, the respective death rates were 22.2 per cent and 60 per cent. The total operative mortality rate in the entire series was 17.3 per cent and the general mortality was 18.9 per cent. The most frequent and serious complications were generalized peritonitis and pulmonary affections. The former occurred in 26 cases with 24 (92.3 per cent) deaths and the latter in 24 cases with 17 (70.8 per cent) deaths.

Harold L. Foss, Danville, Pa.: **Pathogenesis of Thyrotoxicosis With Crisis.**—The results of a study of 90 cases of deaths due to hypothyroidism occurring in a twenty-year period were presented. Lantern slide pictures of many of these cases were shown, the majority of which illustrated the typical appearance of advanced Graves' disease. An analysis of the treatment instituted and the operative procedure employed and the protocols of these cases were made in an attempt to determine the mechanism of acute, hyperthyroid crisis. The author emphasized the fact that, whereas marked progress has been made in the management of hyperthyroidism, deaths in crises still occur in spite of the most careful preoperative preparation and graded operations. Moreover, the exact mechanism remains little understood.

George Crile, Jr., Cleveland, Ohio: **Lateral Aberrant Thyroid Tumors.**—A review of 14 cases of tumors arising in lateral aberrant thyroid tissue was presented. Whereas microscopically the pathologic characteristics of these tumors, which are almost always papillary, are frequently suggestive of carcinoma, clinically they are benign. The author emphasized the fact that these lateral cervical tumors, which are multiple, are primary and not metastatic lesions from the thyroid gland. In one-half the cases papillary tumors of the thyroid were present. Early surgical removal of all involved tissue is advocated. This has resulted in a cure in all of the author's cases. Roentgen therapy is considered ineffective.

Frank H. Lahey, Boston, Mass.: **The Management of True Intrathoracic Goiter.**—The author briefly described the clinical manifestations which may be produced by intrathoracic goiter. These are due, in the main, to interference with the venous drainage of the head and neck because of obstruction to the internal jugular veins and interference with breathing because of pressure upon the trachea. Such goiters are demonstrable by roentgenographic visualization. The technique by which large intrathoracic goiters may be removed without resection of the manubrium was described. This consists of coring out the center of the tumor by the surgeon's finger and thus reducing it in size and making it possible to deliver through the superior thoracic strait. It was necessary to remove the manubrium in only 3 of 365 cases of true intrathoracic goiters operated upon. The author emphasized the value of a rigid intratracheal catheter during operation and the use of helium to increase the amount of oxygen intake during the anesthetic.

Discussion of these three papers was opened by **Frederick A. Coller,** Ann Arbor, Mich., who stated that thyroid crisis was often precipitated by diagnostic procedures before the patient reached the surgeon. Some cases come too late for treatment due to procrastination; in other cases the crises are precipitated by basal metabolic rate readings and by loss of sleep for several days. In this respect he stressed adequate sedation of these cases. He expressed the opinion that often the zealous physician performs too many diagnostic procedures on this type of case. The clinical appearance of the patient should be given preference over all laboratory findings. He also stated that frequently the general appearance of the patient is of greater value than the basal metabolic rate determinations in determining the optimum time for operation.

James H. Means, Boston, Mass., stressed the proper use of iodine in the preparation of toxic thyroid cases and it was his opinion that numerous crises were prevented by its proper use. He agreed with Dr. Foss that the etiology was still unknown. Oxygen and sedation were both important measures in addition to iodine. Hyperthermia occurring in these patients may be combatted by packing in ice. Another important factor which he believed should be stressed is getting the patient in proper psychologic state before surgery is undertaken.

James D. Rives, New Orleans, La., expressed the opinion that in such subtropical centers as New Orleans, the basal metabolic rate reading was probably lower by ten points than in colder climates. He felt that heat and humidity often played a role in precipitating crisis in cases of hyperthyroidism in New Orleans.

W. Bartlett, St. Louis, Mo., stated that the operative risk was best governed by the clinical appearance of the patient and that crises occurred more often in non-operative cases.

REPORT OF THE AMERICAN ORTHOPEDIC ASSOCIATION MEETING AT BUFFALO, N. Y., JUNE 5 TO 8, 1939

W. B. Carrell, M.D., Dallas, Tex.

THE Association met at the home of the President, **W. W. Plummer.** Later in the meeting Dr. Plummer delivered a timely and much appreciated presidential address, outlining the obligations of the Association to the progress of medical science.

The first day of the assembly was devoted to clinical presentations by Dr. Plummer and colleagues. Cases illustrating the end results after various types of operative procedures had been done were shown and freely discussed from the floor.

Of especial interest was a case of transcondylar fracture of the elbow with immediate swelling, loss of radial pulse, and nerve pressure symptoms. Reduction of the fracture and traction failed to relieve, and after three hours a large hematoma was exposed beneath the fascia, which had extended below the elbow and upward to the lower one-third of the arm. On release of the hematoma there was immediate return of the radial pulse and disappearance of numbness in the hand. The wisdom displayed in surgically releasing the pressure from the hematoma prevented Volkmann's ischemia.

The presentation of two cases of traumatic rupture of the biceps tendon at the elbow was interesting because of the rarity of such lesions and the methods employed for repair. Only a few cases, seven, have been previously reported. In both cases the tendon had been avulsed at or near the tubercle of the radius and the free tendon end was found in the elbow fossa. The indications for exploration had been sharp pain on lifting, followed by swelling and loss of function. The method of repair differed in the two cases. It was not anatomically correct in either, but the final function was excellent for all ranges of elbow motion. In one, after failure to adequately expose the radial tubercle, an incision was made in the posterior elbow region and the tendon fastened into the ulna. The muscle so attached was not expected to have supinating power. The patient, however, did have supination power to a full extent, which was attributed to adhesions between the torn fibers of the tendon on the radial tubercle with the tendon passing over it to its new position on the ulna. The other case had the tendon attached to that of the brachialis anticus deep in the elbow fossa. Function was excellent, but the supination power was approximately seventy-five per cent of full strength.

A case of Dupuytren's contracture seventeen years following simple subcutaneous division of the fascia at several points was demonstrated. The palm contained several subcutaneous fibrous masses, but the fingers extended freely

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and the function was good. The method has been used in a considerable number of cases with very satisfactory results. The method essentially is the subcutaneous transverse sectioning of the contracting fascia in the palm and in the fingers affected.

Symposium on Acute Hematogenous Osteomyelitis, arranged by **D. E. Robertson,** Toronto, Ont.—Those participating in the formal discussion were: **J. W. McNeal,** New York, N. Y., **Champ Lyons,** Boston, Mass.; **I. H. Erb,** Toronto, Ont.; **Edwin W. Ryerson,** Chicago, Ill.; **J. Albert Key,** St. Louis, Mo.; and **John Wilson,** Los Angeles, Calif. The historical phases of research study, clinical manifestations, pathology, bacteriology, and treatment were presented by the various speakers.

In summary the present status of available information on this subject may be outlined as follows:

1. The disease is primarily a bacteriemia, and secondarily, a localized lesion in bone.

2. Showers of bacteria in the blood stream usually are cleared quickly, but under certain conditions localize in bone (Lyons).

3. The bacteriemia may, and frequently does, remain in the blood stream as a septicemia.

4. Type of organism: Streptococcus in 50 per cent of children under 2 years of age; over 2 years of age, staphylococcus, 90 per cent (Key).

5. The primary focus of staphylococcus is most frequently a boil, abrasion, or superficial lesion; for streptococcus, more frequently through tonsils or related sources (Ryerson).

6. From primary focus, bacteria enter directly into the blood stream; absence of lymphangeitis at the focus excludes lymphatic route of metastasis (Erb and Lyons).

7. The lesion in bone is a septic thrombophlebitis of the vessels in the metaphysis.

8. The vascular arrangement in metaphysis makes this an ideal bed for localization.

9. Septic thrombophlebitis has been produced experimentally under conditions of reduced virulence of the organism and lowered resistance of the host (McNeal).

10. The resistance in metaphysis comes from the reticuloendothelial cells and the leucocytes (Key).

11. Phagocytosis of bacteria is essential to localization of disease (McNeal).

12. Staphylococci do not produce antibodies in the host, therefore immunity does not exist (Erb).

13. Relation of trauma: Injury near metaphysis, as a wrench of knee, may lower the local resistance, and predispose to infection. Such injury may precede or follow the primary superficial infection. The time limit would not exceed the normal repair from such injury (a few weeks). After such time it may be assumed the particular injury does not relate.

14. Metastasis to other bones, common in osteomyelitis, may result from the primary skin lesion, but more frequently from septic emboli originating at the metaphyseal lesion (Erb).

Treatment—

1. In early stage, general supportive measures to combat a generalized infection.

2. Vaccine does not stimulate antibodies or prevent secondary involvement in other bones; a mass of bacteria and pus in the thrombus is surrounded by three zones; serum does not penetrate the middle zone (Lyons).

3. Serum given early (bacteriemia or septicemia) reduced mortality rate from 70 to 29 per cent in a large group of cases (septicemia) reported by Shands and Baker at American Medical Association meeting not yet published (quoted by Key).

4. Sulfanilamide is of proved value in streptococci infections (Lyons).

5. Sulfanilamide of doubtful value in staphylococci infection. Sulfapyridine used on animals lived longer than controls (Lyons).

Operation Indications.—In this regard there was a variation of opinions as to early or late bone drainage. All agreed that the patient should be given rest, fluids, and transfusions during the early stage. Some would institute drainage immediately on localization (Key); others would delay for several days or longer, waiting for the patient's general reaction to improve (Wilson). The death rate incidence in septicemia was definitely lowered when operation was delayed (Wilson).

The net result demonstrated in the symposium analysis is that we have information regarding the source of infection, bacteriology, and pathology. Further studies should be directed to combating the disease in the generalized stage with more potent serums or some chemical formula as now available for streptococcus. Another problem to be solved is the control of metastasis. Lyons suggested the advisability of ligating the femoral vein when the infection localizes in the lower extremity.

Symposium on Fractures in the Shaft of the Femur, arranged by **Philip D. Wilson,** New York, N. Y.—Those participating formally were: **Frank D. Dickson,** Kansas City, Mo., **A. B. LeMesurier,** Toronto, Can., **Alexander Aitken** and **George W. Van Gorder,** Boston, Mass., **John Dunlop,** Pasadena, Calif., **John R. Moore,** Philadelphia, Pa. **Allen F. Voshell** and **Robert W. Johnson, Jr.,** Baltimore, Md., **William Darrach,** New York, **LeRoy Abbott,** San Francisco, Calif., **H. Winnett Orr,** Lincoln, Neb.

The subject was covered thoroughly in all its aspects. The importance of emergency care was stressed by Dr. Dickson, who reviewed the lessons we learned in war service and their application to civil life. Doctors should give full support to the Red Cross in their work of educating the lay public in emergency care.

Dr. LeMesurier discussed the methods used in Toronto for fractures in children. Very young children are placed on a frame with an inverted U-loop at one end for suspension of both legs. If more traction is desired, the pelvis is strapped down. Older children are also placed on a frame with a Thomas splint fastened to the foot of the bed and skin traction made over a pulley. If the ring is uncomfortable the foot of the bed can be elevated. Dr. Aitken reported a study in 73 cases in children for growth changes following fractures. Those under 12 years of age with over-riding and shortening at the time of treatment have the greatest extent of compensating growth. Some gained 5 to 6 cm. In the series, those under 12 years of age at the time of fracture had at maturity an average 1 cm. longer leg on the affected side. Those over 12 years had 1 cm. shorter leg.

Other speakers reported results in cases treated by skeletal traction, Russell traction, Anderson ambulatory pin, fixation pin and plaster fixation, and finally the elective open operation method. The last championed by Dr. Darrach, emphasized the requirement of firm fixation of two planes, followed by suspension and light traction for early mobilization of joints.

The conclusion seemed obvious that much depends on the surgeon, who must appreciate the problems of reduction and give his personal care in directing the details of traction and splinting. Good results follow many methods if fundamental principles are mastered by the surgeon. Dr. Johnson advised routine chemotherapy combined with good surgery and proper fixation in all compound injuries. Sulfanilamide is given routinely at Johns Hopkins Hospital and the incidence of gas infection has been reduced. "Remember," he said, "SSS, surgery, serum, sulfanilamide in compound wounds."

Dr. Orr discussed compound fractures and advised thorough debridement followed by the best possible reduction and the maintenance of position by plaster and pin fixation in each fragment.

Spondylolisthesis, H. H. Hitchcock, Oakland, Calif.—The author presented a thorough analysis of the lesion, and the paper should be read in detail when published. Three cases were shown with defects of the pedicles, and, following trauma, there was deformity or marked increase in the deformity. Previous reports (other authors) indicate a 5 per cent incidence of defective pedicles in cadaver specimens. In a study of 90 fetuses the author was not able to discover a single incidence. Furthermore, he was able to cause a bilateral separation at the pedicle and lamina junction in fetuses by hyperflexion traumas. He advanced the theory that such traumatic defects, and not accessory ossifying centers, were responsible for spondylolisthesis.

Compression Fractures of the Vertebrae in Diabetes, Mark H. Rogers and **Howard F. Root**, Boston, Mass.—Eight cases of single or multiple compression fractures of the spine were reported. The appearance of the lesions was similar to those found in senile osteoporosis, and in one a malignancy was strongly suspected. Neither phosphatase, calcium, nor phosphorous relations were changed. The common denominator for all was diabetes.

Internal Structure of the Vertebral Body of Man as Related to Health and Disease, George Wagoner, Philadelphia, Pa.—In the study of specimens the essayist correlated the roentgenograms and experimental lesions of the vertebrae. Vertebral bodies are made up of approximately 50 per cent spongiosum. This, in substance, is endothelial tissue with large sinusoidal spaces. The arteries enter through apertures visible in roentgenograms and empty without capillaries into the sinusoidal tissue. Veins return without valves direct to the vena cava. The sinusoidal tissue may be compared with a waterlogged marsh. The H-shaped formation shown in roentgenograms is the vascular system. Lesions of the cortex, unless quite large, are not visible, while very small lesions in the spongiosa show clearly in roentgenograms. This is contrary to the usual interpretations and will necessitate some revision in our analysis of films.

Ununited Fracture of the Neck of the Femur Treated by Combining the Smith-Petersen Nail and Bone Graft Without Opening the Hip Joint, W. E. Gallie and **F. I. Lewis**, Toronto, Ont.—The authors reported fifteen cases of nonunion, operated upon without exposure of the fracture site. Preliminary traction is applied for a few days, using twenty to forty pounds as may be necessary to pull the trochanter to satisfactory position. The operation is approached in manner of a recent fracture procedure. Through the lateral incision a Smith-Petersen nail is applied with firm impaction. Additional drill holes are then made and bone from the ilium is packed in well, for bridging over the fractured area. The nail is used for fixation and the bone graft used only for osteogenesis. More postoperative restrictions are required than in recent fractures. Plaster is not used, but sixty to ninety days' rest is advisable. Results are very good.

A New Approach to the Wrist Joint. Movies to illustrate Arthroplasty with Inert Intervening Material, **M. N. Smith-Petersen,** Boston, Mass.—The operative approach chiefly for wrist fusion includes resection of the lower end of the ulna. The removed bone is finally used for the graft. The subperiosteal exposure gives an excellent view of the wrist joint, and removal of the ulna fragment does not interfere with supination.

Blind Nailing of the T Fracture Lower End of the Humerus Involving the Joint, Oscar Miller, Charlotte, N. C.—The method is applicable only to comminuted fractures of the condyles extending into the joint in adults. None was compounded. The fracture is manipulated, and with the aid of traction, the best restoration possible is secured for the contacting joint surfaces. A Kirschner wire is placed through the medial condyle, and, while holding the lateral condyle firmly, it is likewise transfixed. Two or more additional wires at different planes are inserted and finally all are incorporated in plaster dressing. A few cases were reported, and the reduction and final function were good for this severely comminuted type of fracture.

End Results of Epiphyseal Arrest Operations, C. Howard Hatcher, Chicago, Ill.—Forty-two patients were studied, 14 starting from poliomyelitis, 12 from tuberculosis, and 9 from pyogenic infections. The youngest was 8 years of age; the oldest, 14. Technique used was the method described by Dr. Phemister. Growth expectancy was predetermined by Baldwin tables. Girls reach maturity two years earlier than boys. Children who have a tendency to be tall reach full height earlier. Preadolescent growth is most rapid. An accurate estimate of growth can be made, and 4 to 8 cm. can be secured, depending on number of epiphyses closed. The elective age for operation is 12 years.

Temperature Controlled Healing of Experimental Fractures, Kellogg Speed and **Egbert Fell,** Chicago, Ill.—Work was based on experiments previously reported, those of burying a rat's tail in its own abdominal cavity. The effect of heat on fracture healing was studied in a group of rats with the forearm fractured, the skin reflected, and the foreleg buried in the abdominal cavity. Controls had similar fractures and were treated in splints. Groups of 14-day and 30-day periods were compared. The results were firmer though less exuberant callus, which formed more rapidly than in the control groups.

The Pathology and Treatment of Subdeltoid Bursitis, J. E. Milgrim, New York, N. Y.—Dr. Milgrim reported 142 cases. Some deposits were small, and correct roentgenograms were necessary. Many cases had large masses, filling the subdeltoid fossa. The process is not infective, but is a diffuse degeneration change associated with deposits of calcium carbonate or lipoid bodies. As long as the deposits remain the patient will have recurrence of pain and limited motion. On removal, recovery may be expected. Operative removal is never necessary. Aspiration with a hypodermic needle is quite simple. Some cases with firm deposit should be needled, and when the reaction causes softening, the deposits disappear or may be aspirated.

Spasmodic Torticollis, J. T. Rugh, Philadelphia, Pa.—Organic and functional torticollis should be differentiated. The functional type, from overstimulation of the eleventh cranial, first and second cervical, causes habitual spasm in muscles and is induced by emotional or other irritative factors. Once the pattern is established a long period of rest for the brain cells is necessary. Dr. Rugh's cases, demonstrated by illustrations, proved the efficacy of long periods of fixation. Plaster collars were worn six to twelve months without removal, and with total periods of two to three years in apparatus.

Bone Tumors, Louis Kress, Buffalo, N. Y.—Dr. Kress, by invitation, gave an interesting clinic on primary bone tumors. With projectors placed behind four small screens, the roentgenograms, microphotographic slide, and after results could be viewed simultaneously. The discussion was of a general character and not adaptable to abstracting.

Orthopedic Treatment of Marie-Strumpell Arthritis, Loring T. Swaim, Boston, Mass.—Perseverance and painstaking care characterized the work of the author in his report of eighty-four cases treated in jackets from one to nine years. Deformities of flexion produce strain, not alone on spinal ligaments, but at hips and knees, and induce more extensive ossification. Protection permits better chest expansion, increases resistance, and results in better posture when the disease is quiescent. Jackets must be accurately fitted.

Epiphysitis of the Spine, John G. Kuhns and **Louis Nathan,** Boston, Mass.—In a group of seventy-one cases the results were reported for 25 cases. The youngest was 8½ years old. There were 47 females and 24 males. Faulty posture was present in all; trauma, in 9; multiple lesions of the extremities, in 3. The disability was a defective epiphysis, circulatory or traumatic, involving the cartilaginous plates on the surfaces of the vertebrae. Cases with early and adequate treatment had good posture, although residual changes, such as narrowing of the vertebrae and Schmorl's indentations, were evident in the late roentgenograms. The treatment consisted of the use of extension jackets and bed rest for severe cases, followed by exercises in fixation for a long period. Mild cases were treated by posture exercises alone.

A Further Study of the Head and Neck of the Femur in the Growing Child, W. E. Wolcott, Des Moines, Ia.—A study of the development of the circulation in the head and neck of the femur in infants and children up to 15 years of age was made. Opaque material was injected into the vessels of the ligamentum teres and capsular and nutrient arteries of the shaft of the femur. The following conclusions were reached: (1) In no instance could vessels in the ligamentum teres be demonstrated entering the head of the femur in infants or children under 10 years of age. (2) By injecting the nutrient arteries of the shaft as early as the eighth month of fetal life an anastomosis between this vessel and the capsular vessels was demonstrated. (3) Successful injections into the ossifying center through the capsular arteries, entering the base of the femoral neck, were made as early as 16 months of age. (4) The anastomosis between the capsular and ligamentum teres vessels apparently does not take place until the ossification of the femoral head is nearly complete. It is therefore obvious that circulation through the ligamentum teres does not contribute to the ossifying center in the growing child.

REPORT ON THE MEETINGS OF THE AMERICAN SOCIETY FOR PHARMACOLOGY AND EXPERIMENTAL THERAPEUTICS, INC., TORONTO, ONTARIO, APRIL 26-29, 1939

RAYMOND N. BIETER, M.D., PH.D., ST. PAUL, MINN.

(From the Department of Pharmacology, the University of Minnesota Medical School)

ALLAN D. BASS, from Vanderbilt University, Nashville, Tenn., reported upon an experimental comparison of certain skin-sterilizing agents. A modification of Birkhaug's method, using organisms occurring normally on rabbit's skin, was used. Following removal of the hair, the antiseptic solution was painted on the skin and allowed to dry. Among the results presented were the following data.

DRUG AND CONCENTRATION IN 70% ALCOHOL		% OF STERILE SKIN STRIPS
Mercresin	0.1%	80
Propyl mercuric chloride	0.1%	74.5
Pyridyl mercuric chloride	0.1%	62
Iodine	3.5, 7.0%	55
Merthiolate	0.1%	58
Metaphen	0.5%	55
Mercurochrome	2.0%	51
Ethyl alcohol (control)	70.0%	21-35

In general, the pattern of these results tends to follow other recent publications on this subject. The author noted further that if the antiseptic solutions were rubbed on the skin, their efficiency was increased.

M. H. Seevers and R. T. Stormont, from the University of Wisconsin, Madison, reported upon some of their experiments relative to acapnial hypotension. As is known, hyperventilation in the anesthetized dog or man produces marked arterial hypotension. In the nonanesthetized man or in the dog recovering from cyclopropane anesthesia, hyperventilation produced no arterial hypotension. Later this same dog under cyclopropane showed a blood pressure fall, due to hyperventilation, which was proportional to the depth of narcosis. If, in the anesthetized organism, gastric perfusion was conducted with 0.35 per cent HCl, hyperventilation produced no blood pressure fall. This acid perfusion also partially prevented the characteristic hyperventilation rise in arterial plasma pH. Therefore, these phenomena appear to be due to alkalosis. Their significant conclusion is that anesthesia interferes with chemical and functional readjustment to respiratory alkalosis.

It is well known that morphine administered to dogs produces a marked decrease in the heart rate and that ether subsequently administered leads to a restoration of the normal heart rate; whereas, cyclopropane either produces no change in the slow morphine pulse or else produces a further slowing. **B. H. Robbins, O. G. Fitzhugh, and J. H. Baxter, Jr.**, of Vanderbilt University, Nashville, Tenn., have studied the various factors that may produce these heart rate changes. Using both general anesthetics after morphine administration, they have determined the effects on the heart rate, in normal dogs, in the same animals two weeks after removal of the thoracic sympathetic chains, and then after ligation and excision

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of the adrenals, and, finally, after section of the vagi. The typical slowing of the heart rate due to morphine and cyclopropane occurred after all of the above procedures except section of the vagi. Cutting these nerves abolished the cardiac slowing. Their conclusion is that ether increases the heart rate after morphine in the dog by depressing the vagal system and that cyclopropane augments the effect of morphine on the vagal system.

The abolition of cardiac irregularities observed in dogs after morphine and cyclopropane has also been studied by **J. H. Baxter, Jr., and B. H. Robbins.** These changes, such as bradycardia and ventricular extrasystoles, which were observed with an electrocardiograph, and a fall in blood pressure, occur commonly in dogs, and to a certain extent have also been reported in man. In man these irregularities also occur following the addition of atropine to the morphine before cyclopropane administration. In the dog these changes uniformly occurred before respiratory arrest. If, on the other hand, the dog was also given sodium amytal (2.5 mg. per kilogram of body weight) or sodium barbital, by intravenous injection before the administration of cyclopropane, the cardiac irregularities usually observed did not occur until respiratory arrest. They interpret the effects of these barbitals as being due to depression of vagal tone and a decrease in the irritability of cardiac tissue.

The question of restoring respiratory activity in animals or man depressed by overdose of the hypnotics or general anesthetics is an ever interesting and important subject. Picrotoxin is generally considered to produce the most efficacious respiratory stimulation following barbital overdosage. That this drug does not necessarily produce the best effect in overdose of other depressant substances is shown by the following reports. **H. W. Werner,** of the University of North Dakota, Grand Forks, has studied the effects of a number of drugs in rabbits depressed by overdoses of ethyl alcohol. Coramine, benzedrine sulfate, metrazol, and picrotoxin all increased the minimal lethal dose of alcohol about two times. However, the first three only produced a significant shortening in the duration of alcohol incoordination. Furthermore, coramine and benzedrine sulfate in rabbit alcohol intoxication both produced a greater rise in rectal temperature than did the other two drugs. Possibly this means an increased rate of metabolism of the alcohol. **W. D. Draper and R. W. Whitehead,** of the University of Colorado, Denver, have found in respiratory arrest in dogs produced by overdose of ether that the most satisfactory resuscitation with artificial respiration can be obtained if metrazol is administered before attempts at artificial respiration are commenced.

One afternoon was given over to a symposium on chemotherapy with the American Society of Biological Chemists, Inc. The subject of sulfanilamide and its derivatives was well discussed by a number of speakers. In addition, a number of papers on this subject were presented before the Pharmacological Society. **H. J. White,** of the Johns Hopkins University, Baltimore, Md., reported upon the effect of temperature on the bacteriostatic and bactericidal effects of sulfanilamide and sulfapyridine upon the beta hemolytic streptococcus in vitro. At 30° C. a concentration of sulfanilamide below 1,000 mg. per 100 c.c. was inactive. The activity of the drug increased as the temperature was raised. The most marked bactericidal action was observed at a temperature of 39° C. with a sulfanilamide concentration of 10 mg. per 100 c.c. **A. P. Richardson,** from the same university, reported upon cyanosis in birds and mice due to sulfanilamide. In both species cyanosis was obtained with high blood levels (15 to 118 mg. per 100 c.c. of blood), of the drug. In the mouse the chief effect was the production of sulfhemoglobin. In the bird methemoglobin appeared to be the substance produced. Furthermore, in the bird the intravenous injection of methylene blue reduced the methemoglobin by only approximately 50 per cent for a period of not

over twenty-four hours. **J. T. Litchfield, Jr., H. J. White, and E. K. Marshall, Jr.,** also from Johns Hopkins University, reported upon some very interesting experiments with beta hemolytic streptococcus infections in mice (100 to 1,000 lethal doses per mouse, intraperitoneally) treated with varying blood levels of sulfanilamide. To administer the drug, it was mixed with ground food in varying concentrations. Among the first to use this method with sulfanilamide and its derivatives were **R. N. Bieter, W. P. Larson, E. M. Cranston, and Milton Levine,** at the University of Minnesota, Minneapolis, who used it for studying the effects of various drugs in Type II pneumococcus infections in mice with excellent results. The advantage of this form of drug administration to mice is that there appears to occur an almost continuous absorption of the drug. This is important because of the speed with which these drugs are excreted. The Litchfield, White, and Marshall experiments can best be summarized in the following table:

% OF SULFANILAMIDE IN FOOD	NUMBER OF MICE	BLOOD LEVEL MG. %	% SURVIVAL AT 30 DAYS
0.5	46	7	93
1.0	37	14	81
2.0	45	28	65

It can be seen that a blood level of 7 mg. per cent produced a distinctly superior therapeutic effect. Survival rates that showed these same decreases with feeding increased concentrations of the drugs were reported by Bieter, Larson, Cranston and Levine for Type II pneumococcus infections in mice (4,000 to 8,000 lethal doses per mouse, subcutaneously). With 0.5 per cent sulfanilamide in the food, their survivals at thirty days were 20 per cent; and with 2 per cent, the survivals amounted to 12 per cent. With 0.5 per cent sulfapyridine in the food, 44 per cent of the mice survived; with 1 per cent in the food, 63 per cent of the mice survived; and with 2 per cent of sulfapyridine, only 20 per cent of the mice survived. No determinations of the blood levels of these drugs were conducted by these investigators. These important observations should cause all physicians to consider the question of optimum drug concentrations to use in human therapy. Furthermore, it may be possible to administer too much of these drugs to patients, either without producing distinctly good results, or with the possibility of producing a great measure of harm.

Book Reviews

A Descriptive Atlas of Radiographs. By A. P. Bertwistle, Ed. 4 Pp. 600, with 808 illustrations. St. Louis, 1939, The C. V. Mosby Company. $15.

It is the misfortune of some books to live or be revived beyond the time of their normal usefulness. While this is perhaps pardonable in a work which is characterized by originality and painstaking research, there appears to be no valid reason for a new edition of Bertwistle. Whatever the situation in Great Britain may be, it can safely be said that no physician or medical student in this country is so unfamiliar with radiographs that a collection of miscellaneous reproductions will be of particular value to him. This is even more true when it is considered that the reproductions themselves are in many instances of dubious merit from a photographic standpoint. Despite the author's contention, there is no real correlation with clinical or pathologic findings and the lesions demonstrated are so advanced in grade as to themselves controvert his plea for early diagnosis by means of roentgenography.

Positioning in Radiography. By K. C. Clark. Pp. 450, with 1200 illustrations. St. Louis, 1939, The C. V. Mosby Company. $28.

This is unquestionably the most complete book of its type in English. Practically every useful position and projection is illustrated by photographs clearly demonstrating the method and by exemplary reproductions of radiographs produced thereby. It is difficult to point out any flaw in the work itself which has been most carefully proofread so that few, if any, typographical errors are present. Any criticism which can be raised would be concerned with a lack of flexibility of technique, the exposures being for the most part based on an average patient with no attempt accurately to vary exposures with the actual thickness of the part to be radiographed. The "commercial plug" for Ilford products is not objectionable since that company does no business in this country and since the book is, in a sense, admittedly a house organ. Although the price of the work is high, it is justified by the quality of the paper, the clarity of the illustrations, and the actual size of the volume which is a credit to the publishers.

Gross Anatomy. By A. Brazier Howell, M.D., Johns Hopkins Hospital, Baltimore. Cloth. Pp. 403, with 56 illustrations. New York, 1939, D. Appleton-Century Co. $6.

This is a very difficult book to evaluate. As stated by the author, it is primarily for undergraduate students and is offered as an aid to the student to acquire as much anatomical knowledge as is possible in the shortest length of time. With this objective, we feel that the author has succeeded to a creditable degree. It is well written with accurate and direct descriptions and a very readable style. The underlying principles of gross anatomy are plainly set forth and an effort is made to simplify the complicated anatomy that the student may quickly comprehend it.

Of the many favorable features one should mention the nomenclature. The author has hopefully and wisely compiled simple terms, often using the English equivalents rather than the Latin. A permanent unchanging anatomical nomenclature is something that every doctor dreams of, but the dream will not come true. Histology has been completely omitted and neurology only briefly presented. It is very difficult for those who are wedded to the old school of anatomical teaching to accept the more modern abbreviated instruction in anatomy in which the teaching time has been reduced to 320 hours, as at Johns Hopkins University. With this limited amount of time available, the book undoubtedly satisfies an important need. We are not sure that it can supplement a dissecting guide entirely.

With the addition of more applied embryology, more frequent reference to surgical landmarks and surface anatomy, as well as a more frequent use of diagrams and illustrations, the usefulness of the book would be increased.

One who has not used the book for teaching may find in it many things to criticize. On the other hand, the author's reputation as a teacher of anatomy and his experience with the book in teaching anatomy should recommend it highly.

Del Carcinoma Primitivo Broncopulmonary. By Niceto S. Loizaga, M.D. Paper. Pp. 221, with 20 illustrations. Buenos Aires, 1938, Liberyo y, Editorial "El Ateno."

Primary carcinoma of the lung is receiving increasing attention and recently several treatises have appeared on the subject. During the last ten years at the Francisco Juvier Muniz Hospital in Buenos Aires, there have been forty-six cases of primary carcinoma of the lung, twenty-one of which were available for complete clinical and pathological studies. This 200 page monograph is based upon these observations.

Following an historical résumé of bronchogenic carcinoma, there is a brief consideration of its incidence in which the author demonstrates statistically the increasing frequency of the condition. Much of this is based upon reports in the literature. One chapter is devoted to a consideration of the etiology and pathogenesis in which attention is directed to smoking as a possible factor.

The chapters concerned with the anatomicopathologic and histopathologic characteristics of carcinoma of the lung form the most instructive parts of the book. These are excellently illustrated by photographs of gross and microscopic sections of the various types of lesions. On the basis of these studies the author offers the following classification: (A) cylindrical cell (typical and atypical) bronchial epithelioma; (B) bronchial epithelioma of epidermoid origin (Malpighian and para-Malpighian); (C) atypical bronchial epithelioma (cuboid and small cells); (D) polymorphoepitheliomas; (E) mucoid bronchial epithelioma of glandular origin; (F) alveolar carcinoma (histocytoma of Roger Pilot). The clinical manifestations, roentgenographic characteristics, and other diagnostic laboratory procedures are briefly considered. The book ends with résumés of twenty-eight cases.

The value of this monograph lies in the discussion of the pathologic characteristics of primary lung malignancies. The extensive bibliography is marred by a poor representation of the English and American authors. Moreover, in view of the recent advances in the surgical approach to this problem, a small paragraph devoted to this phase of the subject is obviously inadequate.

Actinomycosis. By Zachary Cope. Ballingbroke Hospital, Wordsworth Common; Late Hunterian Professor and Arris and Gale Lecturer, Royal College of Surgeons. Cloth. Ed. 1. Pp. 248, with 52 illustrations and 17 plates in color. New York, 1938, Oxford University Press. $3.75.

The author of this text is well known to American surgeons for his monographs on acute abdominal disorders which have found wide favor in this country. The author demonstrates again in this text on actinomycosis his ability to relate in a well-ordered manner the significant high lights of the disease. The controversy over the exogenous or endogenous origin of the disease is reviewed and the author inclines to accept the latter; that is, harbored organisms from within the victim's own mouth are a likely source of the contagion.

The chief defect of the monograph would appear to lie in the author's lack of conviction as to what the important agents of the treatment are. In his anxiety for completeness or because of his failure to consider adequately wherein the virtues of a succesful therapeutic agent lie, he leaves the reader somewhat in doubt as to which of the dozen therapeutic agents recommended are the most efficacious. A brief discussion of the principle upon which successful treatment is based would have strengthened this section materially. Nevertheless, the book may be recommended highly to clinicians as a useful source for authoritative information relating to any phase of the clinical problem of actinomycosis.

Physiology of the Uterus. By Samuel R. M. Reynolds. Cloth. Pp. 447, with 44 illustrations, 17 tables. New York, 1939, Paul B. Hoeber, Inc. $7.50.

As the author himself states in the preface to this work: "Up to the present time, it was not been possible for students of physiology, and interested clinicians to find a connected and brief account of what is known of the physiology of uterine muscle." He has prepared such a statement in a very readable and logical form. He has correlated a large volume of anatomical, biochemical, physiologic, and pathologic literature in a reasoned, connected account. There are citations and numerous cross references to the 1,190 papers which constitute the bibliography. The work extends to a conservative discussion of therapy besides covering the field indicated in the title. Although the author disclaims any attempt at exhaustive coverage of the literature, one of the very great merits of the work lies in its richness in this regard. The work also has merit in its clear statement of numerous currently unsolved problems.

The volume is well executed and should serve as a most useful source work in this field of such great clinical and physiologic interest.

A Textbook of Neuro-Radiology. By Cecil P. Q. Wakeley and Alexander Orley. Pp. 336, with 229 illustrations. Baltimore, 1938, William Wood and Company. $8.

A much-needed review of practically all of the well-established data in the field of roentgen diagnosis of the nervous system is here presented. Largely, the book is a compilation from the literature; whole chapters, such as the one on ventriculography, which is based entirely on the work of Lysholm and of David, Mahoudeau, Askenasy, and Brun, are taken from the experience of others. A well-arranged, complete bibliography adds very greatly to the value of the book. The writing is concise and clear and many facts are presented in a short space.

The early chapters cover the technique of roentgen examination of the skull in excellent fashion. Most of the lesions of the calvarium are also splendidly elucidated. On the other hand, skull fractures are inadequately covered. Ventriculography is well brought out, but encephalography receives too little attention. There is a surprisingly extensive description of arterioencephalography and of many of the rarer conditions, such as hydatid and cysticercus calcifications, calcification of the caudate and lenticular nuclei, and others. The chapter on the spine and spinal cord is rather short.

Certain statements are open to question. We would disagree, for example, that myelography in the recumbent position is worthless, that ventriculography is of little value in the meningiomas, or that fractures of the vertebral bodies unite completely in six weeks while fractures of the transverse process commonly unite by fibrous union. Aside from a few such statements, however, the facts presented are substantially correct.

While the diagrams are excellent, the number and the size of the roentgenograms are insufficient. Attention should be called to the error by which the same roentgenogram used in Fig. 72 was apparently repeated in Fig. 74, which illustrates another case.

On the whole this is an authoritative, easily read, well-indexed reference book on neuroradiology which should become indispensable to anyone interested in this field of diagnosis.

Textbook of Pathology. A Correlation of Clinical Observations and Pathological Findings. By Charles W. Duval and Herbert J. Schattenberg, M.D., Tulane University School of Medicine, New Orleans, La. Cloth. Ed. 1. Pp. 681, with 373 illustrations, 13 in color. New York, 1939, D. Appleton-Century. $8.50.

Including the index and the references, there are 681 pages, with 373 illustrations and 13 colored plates. Most of the photomicrographs are satisfactory, but there are many drawings that have a semidiagrammatic appearance. The colored plates of the blood are good.

The authors have presented a rather unfortunate classification of many diseases. Thrombosis, embolism, and infarction are regarded as diseases of the hematopoietic system; edema is a disease of the skin; typhoid fever, trachoma, and undulant fever are diseases of the reticuloendothelial system; while Gaucher's disease and Schüller-Christian's disease (which are truly reticuloendothelial) are classed with the lymphadenomatous system.

There are good discussions of malaria and of leprosy, although the statement is made that *B. leprae* grows readily on artificial media. There are chapters on the pathology of the eye, ear, nose, and throat and a final chapter on the autopsy.

The poorest chapter is the one dealing with nephritis. The old terminology of "chronic interstitial" and "chronic parenchymatous" is used. Fig. 212, labeled acute glomerulonephritis, shows a fairly normal glomerulus; and Fig. 221, labeled chronic parenchymatous, is apparently a hypertensive kidney. The utmost confusion prevails throughout this chapter.

Apart from a few good chapters, the volume is ordinary descriptive pathology of no special merit. The discussions are seldom thorough or fundamental and many important topics are dismissed with scant consideration.